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FOREWORD

We are pleased to make available these proceedings of the first "advanced" training course in PESTICIDES AND PUBLIC HEALTH. This is an additional service of the Division of Pesticide Community Studies that we believe will be of value to you.

Recognition of the need for technical assistance in the development of improved competence in areas relating to pesticides and public health in State and local health departments and in other agencies sharing public health responsibilities led to the first "general" course in PESTICIDES AND PUBLIC HEALTH in May 1967. Response to this course led to the development of a technically oriented course entitled PRINCIPLES OF CHEMICAL EPIDEMIOLOGY, specifically intended for physicians, chemists, and other members of the epidemiological team responsible for investigating illnesses involving chemical agents--this course was first presented in November 1967.

The overwhelming response to these courses led to the decision to offer them annually in Atlanta, Ga., where the headquarters of the Division is located. When demand continued to exceed available facilities and in order to meet a recognized need for training at the local level, a program of field training was developed. The first such course offering PESTICIDES AND PUBLIC HEALTH was conducted in cooperation with the New York City Department of Health in March 1968. Since that time, field training has been an essential part of the Division's program. As of this writing, 35 training courses have been conducted with 2,180 participants--physicians, chemists, scientists, administrators, educators, and businessmen whose interest has been in varying aspects of pesticides and health.

PESTICIDES AND PUBLIC HEALTH, PRINCIPLES OF CHEMICAL EPIDEMIOLOGY, and the field courses have been limited to basic presentations in a core of subjects in pesticides technology, including such areas as air pollution, water pollution, contamination in foods and animals, toxicology and chemistry of pesticides, and safety. Of course we realize that other environmental problems could have been considered; however, limited time and funds required the inclusion of only the highest priority subjects.

There has been a continued desire for more in-depth information on pesticides, both for general knowledge and for use in specific areas. This encouraged us to develop the advanced course in PESTICIDES AND PUBLIC HEALTH. It will be used as a base on which to plan future training in pesticide field technology.

We thank all the distinguished members of the faculty and the attendees for their participation and contributions to this course.

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January 1971

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PERSISTENCE AND FATE OF PESTICIDES IN SOILS, WATER AND CROPS: SIGNIFICANCE TO HUMANS

E. P. Lichtenstein, Ph.D.

To illustrate various principles and points in this presentation, data were used that primarily had been obtained through research in our own laboratory at the University of Wisconsin. This was done for convenience sake only, and many scientists at various institutions are conducting excellent research in this particular field of interest.

Summary

1. The persistence and fate of pesticidal chemicals is dependent on the nature of the chemical itself and a multitude of environmental factors, such as soil types, temperature, light, moisture, microorganisms, etc.
2. It is for these reasons that no absolute "Half-Life" can be attributed to any of these chemicals.
3. The movement of pesticidal chemicals in and through soils is primarily a function of the water solubility of the chemical and of the adsorptive capacities of the soil type.
4. Insecticides like parathion and aldrin adhere to loam soil particles to such an extent that only traces of them could be removed from soils with water. Their presence in water percolated through agricultural loam soils was either nil or far below their water solubility.
5. It appears unlikely that commonly used insecticides are moved within water through soils. They could, however, be transported with washed off soil particles.
6. Insecticides of very low water solubility, such as aldrin, precipitate in mud-water systems and are to some extent being degraded by microbiological processes within the lake or river bottom mud. Soil microorganisms in general, play an important part in the degradation of pesticidal chemicals.
7. Detergents, such as ABS and LAS, prolong the persistence of parathion and diazinon in soil and also have a synergistic effect on both insecticides in soils.

8. Polychlorinated biphenyl plasticizers (P.C.B.) are biologically active substances that apparently prevent detoxification of certain insecticides, thus synergizing their activity. The P.C.B.'s can also interfere with the analyses of certain chlorinated insecticides.
9. The absorption of insecticidal residues from soils into crops is smallest in those soils that contain high percentages of organic matter.
10. The penetration of some insecticides into roots of many plants is large. However, the translocation of these chemicals into the green plant parts is relatively very small.
11. Disruptive effects on the synthesis of DNA, RNA and protein in human cells (HeLa) in tissue culture could be demonstrated with aldrin and DDT at 125 p.p.m., but also with aspirin and sodium chloride. At concentrations of 10 p.p.m., however, these disruptions had mostly disappeared, thus illustrating the problem of dose-response relationship.
12. Concentrated research efforts are needed today that would be directed towards problems related to:
    a) The pharmacological significance of pesticidal residues and other environmental pollutants in human or other biological systems.
    b) The potential interaction of synthetic chemicals on subcellular levels.

The introduction of synthetic pesticides in agriculture gave rise to problems that originally had not been anticipated. In 1952 entomologists in the midwestern United States planned a regional research project whose goal was the determination of the fate of insecticidal chemicals after agricultural usage. Consequently, various field experiments were initiated in 1954 in Wisconsin, Ohio, Kansas and Illinois (Regional Project NC-19). These tests were designed to study the persistence, metabolism and movement of DDT, lindane and aldrin in soils and the potential translocation of these insecticides into the edible parts of crops. Since that time a large amount of data has been accumulated by many research groups in various parts of the world, all indicating the relatively long persistence of certain insecticidal chemicals which have been in use since 1945. In addition, the effects of some of these chemicals on various components of our environment have been studied, pointing at problems which formerly we were not aware of. To obtain data sufficient to produce satisfactory answers for many of these problems, however, is a task of virtually an unsurmountable magnitude. MAN EVENTUALLY WILL HAVE TO TAKE CERTAIN CALCULATED RISKS IF THE USE OF SYNTHETIC AGRICULTURAL CHEMICALS IS TO BE CONTINUED.

The fate and movement of pesticidal chemicals in and from soils is ultimately connected with such expressions as "disappearance" and "persistence" of these chemicals in the environment. The term "disappearance" of a chemical from a certain substrate has been widely used in the past and was in most cases synonymous with the impossibility to detect the originally applied compound where it previously had been applied. This, however, often did not account for the metabolism of the parent compound into other chemicals, which also could be biologically active substances. When we speak of "disappearance" or "loss through volatilization", the parent compound or its metabolites really have not disappeared, except that they have been transported somewhere else.

On the other hand, persistence has to be regarded in relation to the area to which the pesticidal chemical has been applied. This persistence depends on a variety of factors, such as the physical and chemical properties of the chemical itself, the formulation in which it has been applied and the mode of its application to the soil or other target areas. But most important are environmental factors, such as the soil type, soil microorganisms, the presence of other chemicals, temperature, moisture, air movement, light conditions, cover crops, soil cultivation, plant surfaces, etc., (1, 2, 3, 4, 5, 6). Because these factors differ from place to place, it is evident that it is impossible to attribute an absolute life time to any of these chemicals. Dependent on the environmental conditions, they may be of relatively short persistence or may be detectable for a relatively long time.

The term "half life" is frequently employed to indicate the stability or persistence of agricultural chemicals in nature. This term, originally used to measure the rate of radioactive decay can be very misleading when generally applied to pesticides in the environment. The "half life" of any given pesticidal chemical is a function of its chemical nature and the environmental conditions to which it is exposed. These conditions differ from place to place and it is for these reasons that this term should only be used if strictly qualified with a specific description of the environmental conditions. The rate of decline of pesticide residues on or in a given substrate is initially faster than later on (7), thus exhibiting different "half lives" over a given period. This was also demonstrated in 1959 (1) when it was reported that half of the DDT applied at 10 lbs/acre to a loam soil in Wisconsin disappeared within 12 months. This period included 4-5 months of freezing conditions, when probably little or no degradation or loss of the chemical from soil occurred. The decline of the DDT concentration in the loam soil was more rapid during the first 6 months after application than during the following 3 years, and theoretical half life (T 1/2), extrapolated from the rate of decline prior to freezing, was 7.75 months initially. Thereafter, the calculated "half life" for the remaining DDT soil residues was 24.6 months. Depletion curves obtained for aldrin in soils under laboratory conditions indicated 3 to 4 different slopes over a 56-day period (1).

It has been shown that the relative loss of an insecticide from soils (1) or water (8) -- expressed in per cent of the applied dosage -- was to some extent inversely proportional to the initial insecticide concentration, thus indicating that the persistence of a given insecticide is also dependent on its initial concentration in a given material.

To give a general impression regarding pesticide behavior in soils three types of insecticides will be discussed: (I) one of them is a chlorinated hydrocarbon of relatively long persistent properties; (II) the second one is an organophosphorus insecticide of relatively short persistence, but whose various toxic metabolites are the active agents; and (III) the third one is also an organophosphorus insecticide of short persistence properties, but whose metabolites are non-toxic to insects.

I. In a study conducted at the University of Wisconsin (9) the accumulation following treatment and the subsequent decline of aldrin or heptachlor residues in loam soils during a ten-year period (1958-1968) were investigated. Loam soils treated with aldrin or heptachlor at 25 pounds per five-inch acre over the five-year period of 1958 through 1962 contained in the fall of 1968, 4 to 5% of the applied dosages primarily in the form of dieldrin and heptachlor epoxide. Aldrin treated soils also contained photo-dieldrin, which amounted to 1.5% of the recovered dieldrin. In addition, three unidentified, more polar compounds, were detected in these soils, but they were non-toxic to both vinegar flies and houseflies. In addition to gamma chlordane and nonachlor which were present in the original heptachlor formulation, two toxic metabolites (heptachlor epoxide and alpha-chlordane) and three unidentified nontoxic compounds were detected, thus indicating the breakdown in soils of heptachlor and related compounds. All crops grown in these soils contained some insecticidal compounds. Potatoes from aldrin treated soils contained dieldrin (0.047 p.p.m.) and photo-dieldrin (0.0006 p.p.m.), while those grown in heptachlor treated soils contained heptachlor (0.002 p.p.m.), heptachlor epoxide (0.054 p.p.m.), gamma-chlordane (0.015 p.p.m.), alpha-chlordane (0.004 p.p.m.), and nonachlor (0.002 p.p.m.).

II. In another study (10) phorate was incorporated into the upper 5-inch layer of a Carrington silt loam at a rate of 3.2 p.p.m. Soil samples were collected initially, 1, 2, and 5 months later. The residue concentration in these samples as determined by total phosphor analyses amounted to 0.96, 1.42, 0.59, and 0.21 p.p.m. When vinegar flies (Drosophila melanogaster) were exposed for 19 hr. to soil extracts (representing 5 gm of soil each) from these soil samples, mortalities of 100, 89, 65, and 27 percent, respectively, were registered. These toxicities, however, were not due to phorate alone, but also resulted from the presence of the toxic metabolites -- phorate sulfoxide and phorate sulfone.

Tests by thin-layer chromatography revealed that phorate was rapidly oxidized into its sulfoxide and, later, into its sulfone. Phorate was only found in the initial soil sample, which was collected approximately 1 hr. after the insecticidal application. But even at that time, more phorate sulfoxide than phorate was found to be present. This amount of phorate sulfoxide decreased, however, with time, until only traces of this compound could be detected in the 5-month soil sample. Conversely, relatively small amounts of phorate sulfone were present in the initial soil sample, while its concentration increased in soil samples collected at later dates. The mortalities observed after Drosophila flies had been exposed to extracts of phorate-treated soils resulted from the combined toxic action of phorate and its metabolites. These metabolites, however, were not equitoxic and the lethal times to obtain 50 percent mortalities of Drosophila flies exposed to 2-ug quantities of either phorate, phorate sulfoxide, or phorate sulfone were 3, 10 and 6 hrs., respectively.

III. The third example (11) of the fate of an organophosphorus insecticide in soil which was relatively non-persistent and did not produce toxic metabolites, is azinphosmethyl (Guthion). Its persistence and metabolism in soils was studied under field and laboratory conditions. The insecticide was least persistent after field application in an emulsion and when left on the soil surface (50% loss within 12 days after soil treatment) and was most persistent (50% loss within 28 days) after its incorporation in granular form into the upper 4-5 inches of soil. One year after soil treatment with azinphosmethyl granules, 13% of the applied dosage was recovered in the form of azinphosmethyl, and the derivatives mercaptomethyl benzazimide, N-methyl benzazimide and N-methyl benzazimide sulfide or N-methyl benzazimide disulfide. In addition, benzazimide plus 4 unknown compounds were detected. However, toxic effects observed with Drosophila melanogaster Meigen flies or with larvae of the yellow-fever mosquito, Aedes aegypti (L.) were due only to azinphosmethyl. Nearly all the insecticide, although applied at the relative high dosage of 5 lb per acre, was degraded in 1 year into non-toxic products, and more azinphosmethyl derivatives than azinphosmethyl were present at that time. Two years after the insecticidal application, only traces of azinphosmethyl were left in the soil, and concentrations of azinphosmethyl derivatives had also declined.

The amount of ^{14}C-azinphosmethyl applied to soils under laboratory conditions declined over a 10-week period, while the amounts of several nontoxic and more polar derivatives increased during that time.

Volatilization. In previous years, the nondetectability of a particular pesticide has often been equated with "disappearance" or "loss" of the originally applied compound. As research in this field intensified, however, it became evident that pesticidal residues "disappear" through metabolism into other compounds or are transported from the originally treated or contaminated target area such as soils and others. One kind of such movement occurs through volatilization of the chemical. Bowman et al. (12) reported the loss of DDT from aqueous solutions and Lichtenstein and Schulz (4) showed that aldrin was lost from soils through volatilization at a rate which was directly affected by soil moisture. Water had apparently caused a displacement of aldrin from soil particles, thus facilitating volatilization of the insecticide. The authors also showed that the loss of both aldrin and DDT was not affected by the amounts of water evaporated from soils or from glass surfaces, thus indicating that no "co-distillation" took place. These findings were confirmed by Hartley (13).

Spencer (14) stated that "there is no evidence from our data to indicate that the evaporation of water, per se, increases vapor density by a "codistillation" process." He also stated (15) that "the major effect of water on evaporation of such pesticides arises from the increased vapor density due to displacement of the pesticide from the soil surfaces by water." Harris and Lichtenstein (16) described various factors that affect volatilization of insecticide residues from soils under laboratory conditions, while it was shown in field experiments (5) that cover crops, such as alfalfa, considerably reduced the loss of aldrin and heptachlor from a silt loam soil.

The volatilization of four chlorinated hydrocarbon and four organophosphorus insecticides from various substrates over a 24-hr period was recently investigated under laboratory conditions (8). In addition, the volatility of Dyfonate, applied at increasing concentrations to water, was studied over a 24-hr period, and at a fixed concentration over a 10-day period. The rate of volatilization of the various insecticides was a function of the properties of a particular chemical and of the substrate to which the insecticide had been applied. The most volatile insecticide was aldrin, while azinphosmethyl was least. Highest volatilization rates were observed from water while relatively small amounts of insecticides volatilized from soils. Addition of soil, algae, or a detergent to water reduced the volatility of a specific compound in many cases. With increasing concentrations of Dyfonate in water, increasing amounts of the insecticide volatilized from water that had been treated with the insecticide at 2.5 to 20 p.p.m. However, at higher concentrations (40 to 160 p.p.m.) no increase in volatilization occurred. During a 10-day incubation period, increasing amounts of Dyfonate and two unidentified metabolites volatilized from water.

Effect of Microorganisms. Soil microorganisms have a considerable effect on the metabolism or stability of insecticidal chemicals in the soil. It was in 1960 (3) when it was reported that the epoxidation of aldrin or dieldrin in soils was a function of microorganisms. It was found that in aldrin treated soils -- containing a relatively low number of microorganisms (autoclaved loam or Plainfield sand) or in dry soils -- the insecticide not only persisted longer, but the amount of dieldrin produced was only 3 to 10% of the totally recovered residue of aldrin plus dieldrin. In wet loam soil, however, 53% of the totally recovered residue was dieldrin.

The effect of moisture and soil microorganisms on parathion was reported in 1964 (6). The insecticide was most persistent in dry soil and least persistent in soils with a high moisture content. Parathion was not lost through volatilization, as in the case with some insecticides of the chlorinated hydrocarbon group. Degradation of parathion was either by hydrolysis or by reduction to its amino form, depending on populations of soil microorganisms. In soils of low numbers of microorganisms (autoclaved soil) or of low microorganism activity (dry soils), parathion persisted for a relatively long time. No aminoparathion was formed in autoclaved soils. Yeast was primarily responsible for the reduction of parathion in soil to aminoparathion. Bacteria apparently had no effect on this reduction. Paraoxon was hydrolyzed within 12 hr after its application at 20 p.p.m. to a loam soil. During that time, the amount of paraoxon constantly decreased while the amount of p-nitrophenol produced increased. Aminoparathion or p-nitrophenol, added to soils, disappeared within 2 to 16 days, respectively.

Fungi, isolated from an agricultural loam soil, were also tested for their capacity to degrade the insecticides DDT or dieldrin (17). It was found that

Mucor alternans van Tieghen in shake cultures partially degraded DDT within 2 to 4 days into 3 hexane-soluble and 2 water-soluble metabolites. None of these compounds had R_f values that were identical to those observed with DDD (TDE), DDE (1,1-dichloro-2,2-bis (_p_-chlorophenyl) ethylene), DDA (bis-(_p_-chlorophenyl) acetic acid), DBP (4,4'-dichlorobenzophenone), dicofol, and 1,1-bis (_p_-chlorophenyl) ethane. After application of ^{14}C-DDT, 42% of the totally recovered radioactivity was represented by the 2 water-soluble metabolites. Some indication of dieldrin breakdown by the fungus was evident, but no metabolites could be isolated. Degradation of both DDT and dieldrin occurred only with live fungi mycelia, while the insecticides were passively absorbed to dead mycelial controls. After the addition of _M. alternans_ spores to a DDT- or dieldrin-contaminated agricultural loam soil, the insecticide degrading capacity of the fungus was no longer evident. This result was rather disappointing since a need exists to be able to degrade persistent pesticides in nature with soil microorganisms. Since DDE was only found in nonautoclaved soils, its formation from DDT was a function of soil microorganisms.

Movement and Persistence in Water. Concern has been expressed as to the potential movement of insecticidal residues with water from upper soil layers into lower, uncontaminated soil strata. If this would happen, lower water sources could be affected. Lake and river waters can undoubtedly be contaminated through run-off water from adjacent agricultural fields. In this case, though, soil particles to which insecticidal residues are adsorbed are being washed off the soil. However, it has not yet been clearly demonstrated whether water in deeper soil layers can or cannot be contaminated by insecticidal residues. Various experiments were conducted in this respect (18). Insecticide residue levels in soils and water were determined after water had percolated through agricultural loam soils treated previously with parathion or aldrin at 1 p.p.m. Water percolated through these soils contained only parathion residues as evidenced by gas-liquid chromatography and bioassay tests. It appeared that the contamination of water by insecticidal soil residues was to a large degree a function of the water solubility of a particular insecticide. The degree to which water was contaminated was also dependent on the insecticidal concentration in the soil which resulted from the original application dose and the specific properties of a given toxicant in the soil. The vertical movement and persistence of aldrin and parathion in agricultural loam soils were investigated under leaching and non-leaching conditions. The effect of detergents (ABS and LAS) and sodium chloride in water, or of a complete plant nutrient solution on the movement of the insecticides in the soil, was also studied. The water, after its percolation through insecticide treated soil and through lower insecticide free soil layers, was analyzed for insecticidal residues. Quartz sand of no sorptive capacity and minimal microbiological activity was used as a control.

The effects of the sorptive capacities of a loam soil became evident. It was found that water, after its percolation through loam soil that had been treated at a rate of 2 lbs per 6 inch acre, did not contain measurable amounts of aldrin but contained small amounts of parathion. Detergents, after having increased the persistence of parathion in soil, indirectly increased the amount of parathion within the percolated water. Aldrin moved within soils in the absence of percolated water, while parathion moved to a lesser extent. After the percolation of water or water plus LAS through insecticide treated

(20 lbs/6" acre) soil and through lower untreated soil layers, small amounts of aldrin (0.1 to 0.2 p.p.b.) and parathion (0.2 to 0.8 p.p.b.) were found in these water samples. These amounts, though, were far below the water solubility of these insecticides and the water was not toxic to mosquito larvae. The presence of salts prevented the appearance of aldrin residues in the percolated water and reduced the amount of parathion residues. Based on these and other data, it appears unlikely that water in deeper soil layers could be contaminated with insecticidal residues from the upper agricultural soil layers.

Should insecticidal residues contaminate water, the question, of course, arises as to the fate of these residues in water. In this respect, various experiments were conducted (19) and the toxicity of different types of insecticides to mosquito larvae (Aedes aegypti L.) in water and in lake water was determined. Of the chemicals tested, most toxic were parathion and Guthion and least toxic Di-syston and DDT. In additional experiments conducted over a one-year period, the persistence and metabolism of several insecticides in lake water and soil water were determined. This persistence in the two kinds of water was considerably different. The effects of soil water systems, pH, and microbiological activities on the distribution and persistence of aldrin and lindane in water were also studied.

Aldrin precipitated after application to water at 1 p.p.m. The presence of lake-bottom mud enhanced this precipitation. Lindane was stable in water. The presence of soils in water, however, resulted in a partial precipitation of lindane. Once aldrin and lindane reached lake-bottom mud, they were partially broken down. Autoclaving or the addition of sodium azide to mud-water systems resulted in a longer persistence of lindane.

Translocation into Crops. Insecticidal residues in soils present, of course, a potential hazard to the consumer eating crops that were grown in these soils. Many crops have been investigated after growing in insecticide treated soils. It was found that root crops, in particular, contain residues of insecticides, the amount depending on the crop, the soil type and various other conditions (9, 20, 21, 22). The importance of the soil type was further illustrated, when carbon was added to soil to reduce the uptake of insecticidal residues by crop plants (23). In these experiments, peas were grown in the laboratory in aldrin, dieldrin, heptachlor or heptachlor epoxide treated loam soil or quartz sand. Carbon added to soils at 1000 (800 pounds per acre, 3 inches deep), 2000, or 4000 p.p.m. considerably reduced the penetration of the insecticides into the roots and greens of the pea plants. A 96% reduction of the penetration of aldrin into pea roots was achieved with carbon at 1000 p.p.m. in a quartz sand and at 4000 p.p.m. in a loam soil. A 96% reduction of dieldrin or heptachlor and heptachlor epoxide into pea roots was achieved with carbon at 2000 p.p.m. in a loam soil. Carbon in soil prevented the total extraction of the insecticides and reduced the toxicity of the insecticide residues to *Drosophila melanogaster* Meigen. This binding of the residues to the carbon-soil complex increased with time. Field test results, although similar, were not so striking as in the laboratory. Treatment of the soil with carbon could reduce insecticidal residues in crops to such an extent that a farmer could use a soil of abnormally high insecticidal content. Data obtained in 1968 clearly indicated (9) that various crops absorb an insecticide at different rates from the soil and that one crop absorbs different insecticides in the soil at different rates. Field soils used in this study contained in the fall of 1968 heptachlor and heptachlor epoxide at a concentration of 0.7 p.p.m. and gamma-chlordane at a concentration of 0.82 p.p.m.

Although more gamma-chlordane than heptachlor epoxide was present in the soil, the amounts of gamma-chlordane in crops were only one fourth of the heptachlor epoxide concentration. Proportionally more heptachlor epoxide than gamma-chlordane had been absorbed by these vegetables (carrots, potatoes, beets, radishes, cucumbers).

Once insecticides penetrate into plant tissues, they can be further metabolized by plant enzymes. This was illustrated when subcellular fractions from peas were obtained by differential centrifugation after the plants had been grown under both sterile and nonsterile conditions (24). Enzymatic conversion of aldrin to dieldrin was achieved with different cell fractions. Of the total dieldrin recovered from all cell fractions, 11% was produced by the "nuclei"-pellet (1000 G), 18% by the "mitochondria"-pellet (10,000 G), 17% by the "microsome"-pellet and 54% by the soluble fraction (105,000 G). The enzymatic activity was increased with Cu^{2+} and Fe^{2+} by 123 and 56%, and was inhibited by Mn^{2+}, sesamex, and SKF 525-A by 30, 72, and 80%, respectively. The effects of Cu^{2+} and Fe^{2+} could be nullified by the addition of EDTA to the reaction mixtures. The enzyme(s) in peas appeared different from that described in animal tissues since: it is specific for aldrin and did not epoxidize the endo-endo isomer of aldrin (isodrin) or heptachlor; cofactors, such as NAD, NADP, and NADPH did not affect the rate of epoxidation of aldrin; and most of the enzymatic activity was found in the soluble fraction and not in the "microsome"-pellet.

Significance of Residues. Finally, the significance of pesticidal residues in the food chains of man and animals remains as one of the most controversial problems. Figures in Table 1, compiled from the Handbook of Analytical Toxicology (25) clearly show that insecticide residues are present in human tissues.

But we also consume naturally occurring toxicants, as illustrated with the two insecticidal compounds 2-phenylethylisothiocyanate (26, 27) and myristicin (28). The first one is present in the edible parts of turnips and other cruciferous crops while myristicin is found in the edible parts of parsnips. Both naturally occurring compounds also exhibited mammalian toxicities (Table 2). Experiments were also conducted in our laboratory with HeLa cells (29), an established cell line originally isolated from a human uterine cervical carcinoma. Monolayer cultures of these HeLa cells were used to study the toxicity of selected organophosphorus (parathion, diazinon, Di-syston), chlorinated (DDT, aldrin, dieldrin), and carbamate (Carbaryl, Temik (Union Carbide)) insecticides and some of their potential metabolites. Dosages causing 50% inhibition of cell culture growth (ID_{50}) were determined and the effects of the insecticide on synthesis of nucleic acids and proteins were studied. With chlorinated and carbamate insecticides, ID_{50} values varied inversely with the compound's water solubility. After 4.5 hours of incubation at 10 p.p.m., only diazinon had a deleterious effect on DNA synthesis and only DDT affected RNA synthesis while Di-syston was the only compound affecting protein synthesis. At 125 p.p.m., aldrin and DDT showed significant disruptions on all three variables, while parathion at its ID_{50} dose showed no effect on any variable. Exposure of HeLa cells to aspirin or sodium chloride resulted in effects that were similar to those observed with some of the insecticides. The problem of dose-response relationship is particularly demonstrated by these data.

In another study (30) the toxicity of various environmental chemicals was determined using both malignant (HeLa cells) and non-malignant (skin fibroblasts) human cells in tissue culture. Aspirin, caffeine, an industrial polychlorinated biphenyl plasticizer (Aroclor^{R} 1254), carbaryl, DDT, parathion and several insecticide metabolites were studied for their effect on the growth of human cells in tissue culture. The dosage causing a 50% inhibition of culture growth (ID_{50}) was determined and the ability of these environmental chemicals to interact and their potential effects on the synthesis of nucleic acids and protein was determined. Both cell types responded nearly equally to the presence of an individual chemical. Aspirin and caffeine were 8-20 times less toxic than any of the other chemicals studied while the plasticizer was as toxic as was DDT. Studies with insecticide metabolites indicated that paraoxon was less toxic than parathion and that p-nitrophenol was as toxic as was parathion. Alpha-naphthol was less toxic than its parent compound, carbaryl. The toxicities of DDT and DDE were dependent upon the cell type. Little significant interaction on DNA, RNA or protein synthesis was seen with either cell type.

Comparing the acute toxicities (Table 2) of DDT and of the naturally occurring insecticidal substances that were isolated from turnips and parsnips with the toxicities of some drugs (25) the problem of dose-response relationship arises. We should remember, however, that two basic differences exist between an insecticide such as DDT in our food and drugs. While we do not control the intake of insecticidal chemicals with our food, we do control the intake of drugs. Moreover, many insecticidal residues in our food are not water soluble or have an extremely low water solubility and are stored in animal fat. The drugs mentioned in Table 2, however, are water soluble and readily excreted.

Finally, I would like to emphasize the importance of establishing the pharmacological significance of pesticidal residues and other environmental chemicals in human or other biological systems. It is for this reason that the increasing interest of medically trained researchers in the field of biologically active substances -- such as pesticides, drugs, etc. and their action and interactions in living systems -- is rather encouraging.

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Table 1. Insecticide Concentrations in Humans, p.p.m. (1960-1969 Averages, Handbook of Anal. Toxicol).

	Fat	Plasma	Urine
p,p'-DDT	4.10	0.016	0.007
Dieldrin	0.215	0.008	0.016
Lindane	<0.01	< 0.001	< 0.001
Heptachlor epoxide	0.15	0.001	< 0.001

Table 2. Acute Toxicities: LD-50, mg/kg.

	Oral	Intravenous
p,p'-DDT	300-M[a/]	50-R[b/]
2-phenylethylisocyanate	700-M	50-M
Myristicin	1000-M	200-M
Aspirin	1100-M	500-M[c/]
Caffeine	200-M	100-M
Amphetamine	38-M	14-M
Phenobarbital	325-M	175-M

a/ = Mouse, b/ = Rat, c/ = Intraperitoneal

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SOIL CHEMISTRY OF PESTICIDES

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The fate of chemicals in soils is a subject of current national interest due to its potential role in environmental pollution. Agricultural pesticides have been singled out for special consideration since large quantities are being dispersed on major agricultural soils. As a consequence, soils represent a vast reservoir receiving pesticides applied either intentionally or accidentally.

Pesticides are classified according to the target organism they control. The following five major classes generally recognized are *herbicides*, *insecticides*, *fungicides*, *nematicides*, and a small group composed of defoliants, desiccants, and growth regulators. In addition there are a limited number of chemicals used as miticides, rodenticides, repellents, and other pest control agents. The most reliable figures indicate that approx 119 million acres are sprayed for weed control (herbicides), 97 million acres are treated for insect control (insecticides), and about 25 million are treated for plant diseases (fungicides), for nematodes, or with defoliants, desiccants, or growth regulators (1). If one calculates that about 340 million acres of soil are under cultivation in the continental United States, then a large percentage of our most fertile soils are receiving one or more applications on a seasonal basis. See Fungicides; Insecticides; Weed killers; Poisons, economic; and Plant growth substances.

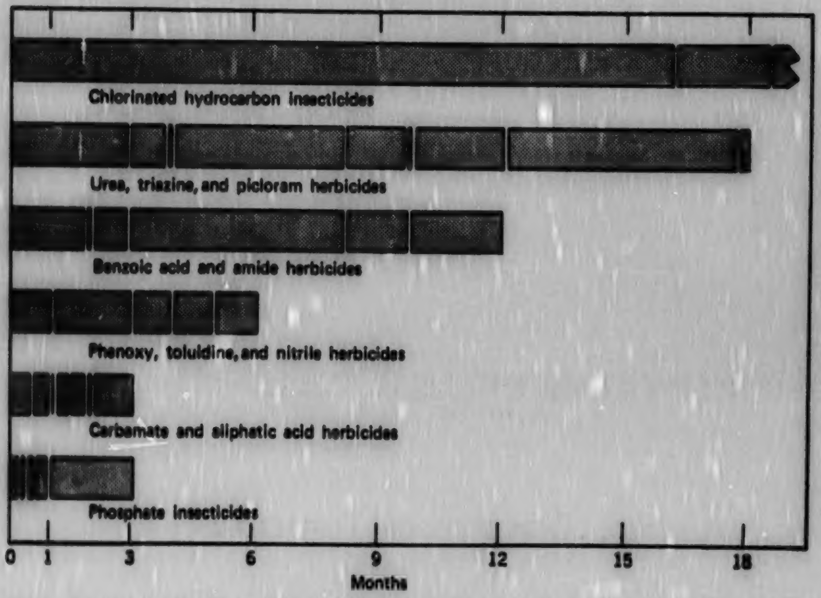


Fig. 1. Persistence of twelve major classes of pesticides in soils. Each bar represents one or more major class of pesticide; the open spaces represent individual pesticides in that major class; and the length of each bar represents the time required for a 75–100% loss of the pesticide as measured in months (2). Courtesy Charles C Thomas, Publisher, Fort Lauderdale, Fla.

Most research on pesticides in soils has centered on residual members of the first two classes of pesticides. The chlorinated hydrocarbon insecticides represent the most persistent class of pesticides. Under normal usage conditions, most polychlorinated insecticides remain in soil 2–5 years (Figs. 1 and 2). In contrast, many highly toxic phosphate esters decompose in a few months and consequently pose no residual problem (Fig. 2). The organic herbicides exhibit a wide spectrum of persistence, which may range from several days up to two years (Fig. 2).

One problem caused by residual pesticides in soils stems from the capacity of many plant species to absorb and translocate these materials into food and fiber products.

Table 1. Production and Sales of Pesticides in the United States in 1967 (4)

Type of pesticide	Quantity of pesticide, 1000 lb	Value, $1000	Unit value,* $
fungicides	120,413	56,333	0.37, 0.67
herbicides and plant hormones	287,582	429,980	1.55, 1.15
insecticides, rodenticides, soil conditioners, and fumigants	489,368	300,730	0.60, 0.64
total	897,363	787,043	0.92

*For cyclic and acyclic pesticides, respectively.

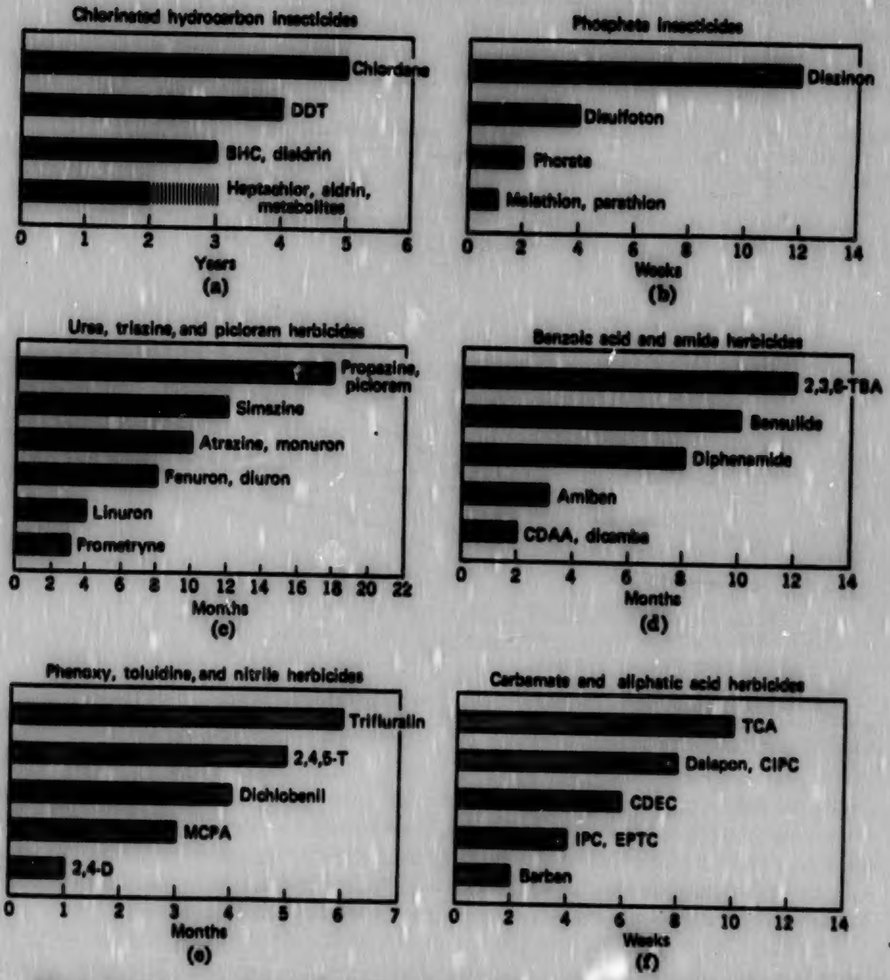


Fig. 2. Persistence of thirty-eight individual pesticides in soils. The broken black area after heptachlor and aldrin represents the additional insecticidal persistence caused by their respective metabolites, heptachlor epoxide and dieldrin (2). Courtesy Charles C Thomas, Publisher, Fort Lauderdale, Fla.

To keep abreast of the content of pesticides in soils and in other phases of the environment, extensive monitoring programs are conducted by the Government. Areas of high pesticide usage are monitored intensively to determine whether progressive accumulation is occurring. Market basket surveys, based on the diet of a 19-year-old male, are conducted periodically by the Food and Drug Administration. Surveys thus far indicate most samples contain residues well below established pesticide tolerances, and that only 3% of the total foods analyzed are above these established tolerances (3).

Residual pesticides in soils may present an additional problem from an agronomic and environmental standpoint. For example, residual herbicides have damaged crops

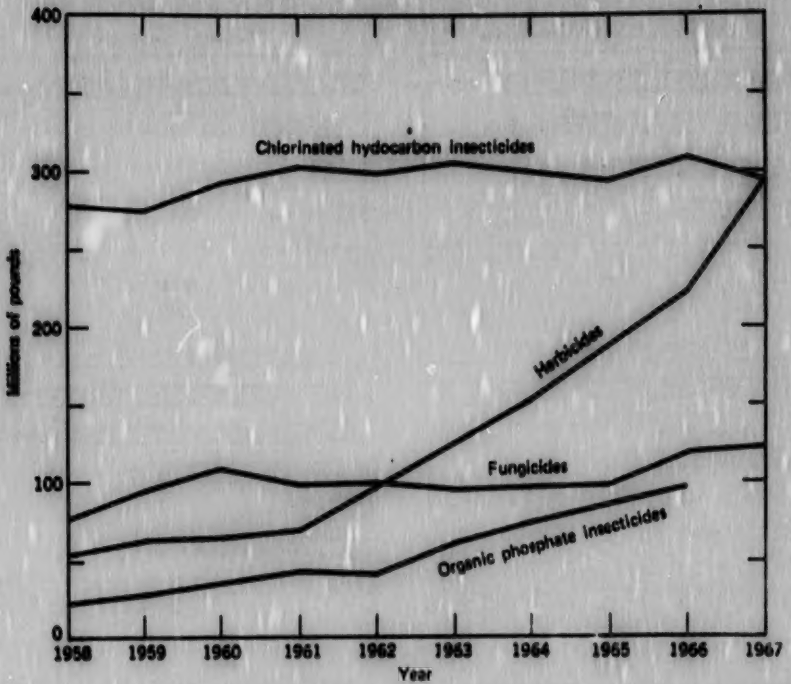


Fig. 3. Organic pesticide chemicals sold annually in the United States. Values are in millions of pounds of technical products. Values for organic phosphate insecticides in 1967 are not shown. Adapted from (4).

grown the following year. Residual insecticides have found their way into water, and consequently have affected marine life and their predators. As a further consequence, some reproductive failures have been reported in birds feeding on fish contaminated with the chlorinated hydrocarbon insecticides. The incidence of pesticides in wildlife is also being closely monitored in Government surveys.

Before considering in detail the chemical aspects of pesticides in soils, some information on the scope of the pesticide industry may be helpful. The total sales of pesticides have increased steadily over the past decade (Fig. 3). The total sales of chlorinated hydrocarbon insecticides have remained fairly stable during this period: In contrast, the herbicides have enjoyed considerable growth in total sales in this same period. Current trends indicate that herbicide and fungicide usage will remain fairly constant. The total production and sales of synthetic organic pesticides in the United States in 1967 are shown in Table 1 (see p. 516).

Chemistry of the Pesticides

Excellent reviews of the properties of selected pesticides may be found in the series by Metcalf (5) and in the text by Crafts (6). Any detailed consideration of the pesticides is difficult, since there are over 125 herbicides, 90 insecticides, and numerous other pest control agents presently being marketed. A list of the common and chemical names of the pesticides cited in the present text is found in Table 2.

Table 2. Chemical Designations of Pesticides Mentioned in Text

Common name	Type of pesticide[a]	Chemical name
aldrin	I	1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4-*endo-exo*-5,8-dimethanonaphthalene
amiben	H	3-amino-2,5-dichlorobenzoic acid
amitrole	H	3-amino-1,2,4-triazole
atrazine	H	2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine
Banol[b]	I	6-chloro-3,4-xylyl *N*-methylcarbamate
barban	H	4-chloro-3-butynyl *m*-chlorocarbanilate
Baygon[b]	I	2-isopropoxyphenyl *N*-methylcarbamate
bensulide	H	*N*-(2-mercaptoethyl)benzenesulfonamide
γ-BHC	I	see lindane
cacodylic acid	H	dimethylarsinic acid
captan	F	*N*-trichloromethylmercapto-4-cyclohexene-1,2-dicarboximide
carbaryl	I	1-naphthyl *N*-methylcarbamate
CDAA	H	*N*,*N*-diallyl-2-chloroacetamide
CDEC	H	*S*-2-chloroallyl *N*,*N*-diethyldithiocarbamate
chlordane	I	1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene (principal constituent)
chloroxuron	H	3-[*p*-(*p*-chlorophenoxy)phenyl]-1,1-dimethylurea
CIPC	H	isopropyl *m*-chlorocarbanilate
dalapon	H	2,2-dichloropropionic acid
2,4-D	H	2,4-dichlorophenoxyacetic acid
2,4-DB	H	4-(2,4-dichlorophenoxy)butyric acid
DDD	I	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane
DDE	I	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethene
DDT:	I	mixture of following two:
p,p′-DDT		1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane
o,p′-DDT		1,1,1-trichloro-2-(*o*-chlorophenyl)-2-(*p*-chlorophenyl)ethane
diazinon	I	*O*,*O*-diethyl *O*-2-isopropyl-6-methyl-4-pyrimidinyl phosphorothioate
dicamba	H	3,6-dichloro-*o*-anisic acid
dichlobenil	H	2,6-dichlorobenzonitrile
dieldrin	I	1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,-7,8,8a,-octahydro-1,4-*endo-exo*-5,8-dimethanonaphthalene
diphenamid	H	*N*,*N*-dimethyl-2,2-diphenylacetamide
diquat	H	6,7-dihydrodipyrido[1,2-*a*:2′,1′-*c*]-pyrazidinium salt
disyston	I	see disulfoton
disulfoton	I	*O*,*O*-ethyl *S*-2(ethylthio)ethyl phosphorodithioate
diuron	H	3-(3,4-dichlorophenyl)-1,1-dimethylurea
DNBP	H	4,6-dinitro-*o*-*sec*-butylphenol
DSMA	H	disodium methanearsonate
endrin		1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,-7,8,8a-octahydro-1,4-*endo-endo*-5,8-dimethanonaphthalene

(continued)

Table 2 (*continued*)

Common name	Type of pesticide[a]	Chemical name
EPTC	H	*S*-ethyl *N*,*N*-dipropylthiocarbamate
fenac	H	2,3,6-trichlorophenylacetic acid
fenuron	H	1,1-dimethyl-3-phenylurea
ferbam	F	ferric dimethyldithiocarbamate
fluometuron	H	1,1-dimethyl-3-(α,α,α-trifluoro-*m*-tolyl)urea
heptachlor	I	1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene
heptachlor epoxide	I	1,4,5,6,7,8,8-heptachloro-2,3-epoxy-2,3,3a,7a-tetrahydro-4,7-methanoindene
IPC	H	isopropyl carbanilate
isodrin	I	1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4-*endo-endo*-5,8-dimethanonaphthalene
lindane	I	γ-1,2,3,4,5,6-hexachlorocyclohexane
linuron	H	3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea
malathion	I	*S*-[1,2-bis(ethoxycarbonyl)ethyl] *O*,*O*-dimethyl phosphorodithioate
Matacil[b]	I	4-dimethylamino-*m*-tolyl *N*-methylcarbamate
Mesurol[b]	I	4-(methylthio)-3,5-xylyl *N*-methylcarbamate
MCPA	H	4-chloro-2-methylphenoxyacetic acid
metobromuron	H	3-(*p*-bromophenyl)-1-methoxy-1-methylurea
monuron	H	3-(*p*-chlorophenyl)-1,1-dimethylurea
nabam	F	sodium ethylenebisdithiocarbamate
nitralin	H	4-(methylsulfonyl)-2,6-dinitro-*N*,*N*-dipropylaniline
paraoxon	I	*O*,*O*-diethyl *O*-*p*-nitrophenyl phosphate
paraquat	H	1,1′-dimethyl-4,4′-bipyridinium salt
parathion	I	*O*,*O*-diethyl *O*-*p*-nitrophenyl phosphorothioate
phorate	I	*O*,*O*-diethyl *S*-[(ethylthio)methyl] phosphorodithioate
picloram	H	4-amino-3,5,6-trichloropicolinic acid
prometryne	H	2,4-bis(isopropylamino)-6-methylthio-*s*-triazine
propanil	H	3′,4′-dichloropropionanilide
propazine	H	2-chloro-4,6-bis(isopropylamino)-*s*-triazine
Semesan[c]	F	hydroxymercurichlorophenol
simazine	H	2-chloro-4,6-bis(ethylamino)-*s*-triazine
2,4,5-T	H	2,4,5-trichlorophenoxyacetic acid
2,3,6-TBA	H	2,3,6-trichlorobenzoic acid
TCA	H	trichloroacetic acid
trifluralin	H	α,α,α-trifluoro-2,6-dinitro-*N*,*N*-dipropyl-*p*-toluidine
vernolate	H	*S*-propyl *N*,*N*-dipropylthiocarbamate
Zectran[d]	I	4-dimethylamino-3,5-xylyl *N*-methylcarbamate

[a] NOTE: I, insecticide; H, herbicide; F, fungicide.
[b] Registered trademark of Farbenfabriken Bayer AG.
[c] Registered trademark of E. I. du Pont de Nemours & Co., Inc.
[d] Registered trademark of Dow Chemical Co.

Processes Acting on Pesticides in Soils

The processes acting on a pesticide in the soil environment can be roughly subdivided into three major areas: physical, biological, and chemical although some ambiguity exists about the specific processes to be listed under these major headings.

Under the physical processes may be listed photodecomposition, or alterations on the soil surface by ultraviolet radiation; volatilization, or movement in the vapor phase; leaching, or movement by capillary water into the soil profile; and physical adsorption onto various soil colloids. Under biological processes may be listed metabolism by soil microorganisms and root uptake, or absorption by the plant. Under chemical processes are included all reactions not mediated by the soil microorganisms, ie, those reactions catalyzed by various soil components and chemical adsorption. Finally, it must be realized that several of these processes are operating in concert on any particular pesticide and often they cannot be considered independently.

No accurate balance sheet has yet been devised for the contribution of each of these processes for a given pesticide in the soil. The persistence values given in Figures 1 and 2 indicate that some of these processes are extremely slow. The effective life of a pesticide in soil depends on the chemical properties of the molecule and the properties of the surrounding soil. At the soil surface, photodecomposition and volatilization are probably important; the remaining processes come into play after the molecule moves beneath the soil surface. Therefore, the time a molecule remains on the surface versus the time it remains in the soil proper is an important consideration as to its fate. Many pesticides are incorporated directly into the soil to prevent rapid losses due to volatilization and photodecomposition.

In the following sections, two of the better understood processes affecting pesticides will be discussed. Next, reactions dealing with the insecticides, herbicides, arsenical pesticides, and fungicides will be considered.

Adsorption. A variety of soil factors complicate prediction of a given pesticide's behavior. Furthermore, there are thousands of soil types in the United States, each differing in physical or chemical characteristics and subject to substantial differences in climate. These soil–climate parameters explain the greater effectiveness of a pesticide on a sandy soil compared to a neighboring clay loam and the greater persistence of certain herbicides in the cooler temperate regions than in semitropical areas. The complexity of soil factors is perhaps best seen in the adsorption of pesticides.

One of the most important physical or chemical processes governing pesticide behavior within soil is adsorption, ie, concentration at or exclusion from the solid surface. Adsorption directly or indirectly influences pesticide movement, photodecomposition, plant uptake, microbial and chemical decomposition, and volatilization. Compounds strongly adsorbed by soil components are not readily moved by water passing into and within the soil. When applied at the surface, such pesticides are more susceptible to photodegradation and volatilization. Organic cations such as paraquat and diquat are adsorbed so strongly that phytotoxicity is virtually eliminated in soils other than sands.

Adsorption of organic pesticides by soil colloids has been thoroughly reviewed by Bailey and White (7). Adsorption may arise from coulombic attraction, dipole interactions (van der Waals forces), or hydrogen bonding. Energy of adsorption is the summation of these forces: In general, van der Waals adsorption is weak and coulombic attraction strong.

The most significant soil factors governing adsorption behavior of a pesticide are the nature and amount of the soil components. Soil organic matter usually is the component most highly correlated with adsorption, loss of pesticide bioactivity, retention against leaching, and the like. Organic matter has a high adsorptive capacity for cationic pesticides because of its pH-dependent net negative charge, and for neutral molecules because of physical adsorption. In the latter category adsorption of chlorinated hydrocarbon insecticides, eg, aldrin, DDT, γ-BHC, increased with higher organic matter content and, to a lesser extent, clay content. Increased moisture content may decrease adsorption, enhancing bioactivity of certain insecticides. Adsorption and movement of neutral pesticides in soils have been treated as a partition-chromatographic process. Organic matter is considered the stationary phase: The "active fraction" of organic matter, or that portion which participates in the sorption process, can be determined experimentally. The adsorptive capacity of the soil organic matter is then measurable and designated as omega (Ω). The use of a distribution constant based on Ω is then a true constant, independent of soil type (8).

The second major soil component affecting adsorption is the mineral fraction. The crystalline layer silicate clays such as montmorillonite and vermiculite are of greatest importance because of their high cation exchange capacities (80–150 meq/100 g) and surface areas (600–800 m^2/g). In addition, kaolinite, halloysite, illite, chlorite, and interstratified variations of the clay minerals contribute further to adsorption capacity. See Clays.

Though often overlooked, oxides and hydroxides of iron and aluminum may contribute significantly to the soil chemistry of pesticides by development of a pH-dependent positive charge, coupled with high surface area. They are especially abundant in highly weathered soils such as those in tropical and semitropical regions of high rainfall. Thus, picloram is strongly adsorbed by hydrated metal oxides and a red lateritic soil, but poorly adsorbed by montmorillonite, kaolinite, attapulgite, and purified illite (9). Low pH and high organic matter also favor adsorption of picloram and other acidic herbicides, such as 2,4-D and 2,4,5-T.

Both adsorbent and adsorbate may be influenced by soil pH. At very low pH a variety of organic compounds are strongly adsorbed to montmorillonite, kaolinite, and illite (10). Anionic herbicides (2,4-D, 2,4,5-T, MCPA) are negatively adsorbed at pH greater than 6–7. Ion exchange resins and other polymers, often studied as model soil components, exhibit greatest adsorption of ureas and triazines at low pH.

Current research emphasis in pesticide adsorption is shifting from measurement of adsorption–desorption isotherms to elucidation of the adsorption mechanism. To this end, infrared spectroscopy appears to be the most promising technique.

Photodecomposition. Decomposition by light plays some part in the transformation of pesticides in the environment although the practical significance of this method of decomposition is difficult to assess quantitatively. Absorption of light by pesticides is a surface phenomenon which may occur on soil or leaf surfaces. One of the prime factors determining the readiness of a pesticide to decompose in sunlight is its absorption spectrum. Many pesticides are substituted aromatic compounds and have absorption maxima between 200 and 350 $m\mu$, that is to say, in the near ultraviolet range. Sunlight is a poor source of such radiation since it contains negligible radiation of a wavelength less than 295 $m\mu$. Consequently, solar energy is usually insufficient to effect direct fission of covalent bonds. However, many reactions do occur in aqueous solutions of pesticides receiving solar radiation although the precise mechanism by which energy transfer takes place requires further study. Additional information concerning the nature of sensitized processes and photolysis in the solid and adsorbed states is required. Contact of pesticides with trace metals and the proximity of naturally occurring complex organic compounds present in soil or leaf constituents provide favorable situations for energy transfer. In these circumstances the production of oxygenated or reduced derivatives may depend on the proximity of oxygen or hydrogen sources to the activated molecule.

The complexity of the natural environment has restricted photochemical studies primarily to the investigation of the products of photolysis in solution or as solid films. Often the study of photodecomposition has been undertaken to determine the loss of biological activity following irradiation. The rate of bioactivity loss reflects the rate of photodecomposition but affords little other chemical information.

Many organic pesticides are complex molecules and contain a number of functional groups. Photochemical reactions of individual groups are often predictable by reference to previously investigated models since even in a more complex molecular environment similar reactions may occur. However, the relative reactivity of functional groups becomes extremely difficult to predict. The replacement of a halogen atom by hydroxyl (or occasionally by hydrogen) in aqueous solution or by hydrogen in a hydrogen donor solvent, eg, methanol, is frequently observed when halogen atoms are bonded to an aromatic ring system. Photoreactivity of halogen atoms attached to an isolated double bond is observed in the cyclodiene insecticides. New carbon–carbon bonds are formed at the site of departure of the chlorine atom or reduction may occur in a hydrogen donor solvent at greater dilution.

Photooxidation usually transforms amines and phenols into dark-colored materials of high molecular weight. In aqueous solution halogenated phenoxyaliphatic acids generate polyhydroxyphenols photolytically by ether fission and replacement of halogen by hydroxyl. Since polyhydroxyphenols are extremely susceptible to oxidation at low pH, the resultant phenols readily polymerize and can only be isolated if their further oxidation is inhibited. It should be borne in mind that polyphenols (and many other classes of compounds generated by photolysis) are very reactive and can therefore be isolated from the reaction mixture only with difficulty. Another reaction of sufficient generality is the removal of alkyl or alkoxy groups attached to nitrogen atoms.

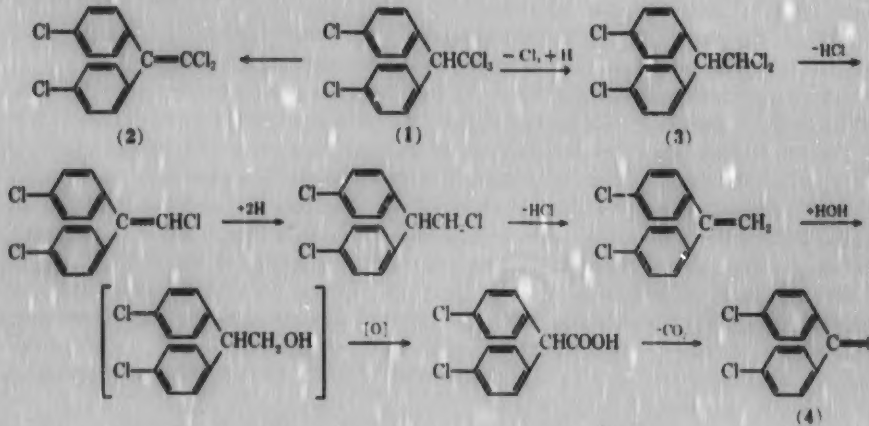
Several texts on organic photochemistry (11,12) are available and provide an excellent foundation for understanding the photochemistry of pesticides. However, predictions based on extrapolation from the photochemical behavior of a model system will be of limited value until broader knowledge of the effect of many complicating factors can be accumulated.

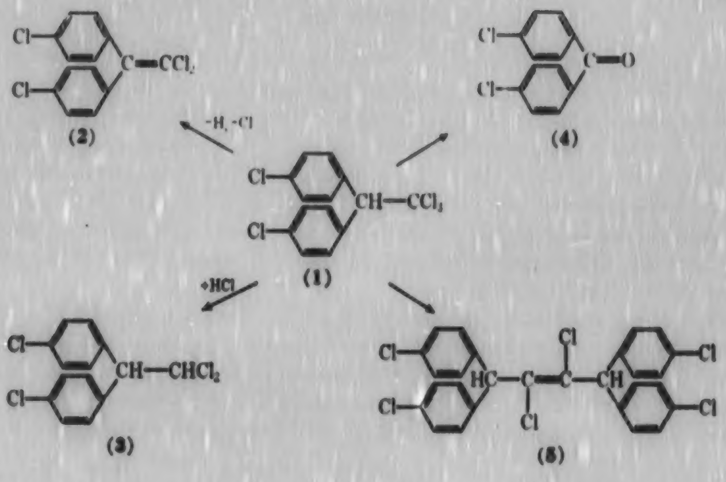
Insecticides

Three major classes of insecticides have been studied in soil: the *chlorinated hydrocarbons* (DDT, aldrin, dieldrin, endrin, heptachlor); the *organic phosphates* (malathion, parathion, diazinon); and the *methyl carbamates* (carbaryl, Banol, Baygon). Only the chlorinated hydrocarbons persist in soils (Fig. 1). Reported values for their rates of disappearance differ. Soils receiving high initial rates of application have been reported to contain 40–45% of the original material after 14 years (13). The low solubility of most of the chlorinated hydrocarbon insecticides probably contributes to their stability in soils. Other factors influencing their persistence are rate of application, moisture, pH, and microbial activity.

DDT. Total worldwide production of DDT since its introduction has been estimated at over 3.5 billion lb (4). Because of its extensive use in crop protection programs DDT is the pesticide most frequently found in soils. Due to its low solubility, DDT does not leach rapidly in soils. Because DDT is so extremely hydrophobic, it exhibits some interesting properties in water. DDT molecules in water tend to migrate to the surface. At this air-water interface, DDT evaporates with water molecules faster than would be predicted from its extremely low vapor pressure. The occurrence of DDT in untreated areas throughout the world may be a consequence of this ability to evaporate with water vapor. Two processes that alter this insecticide are microbial metabolism and photodecomposition.

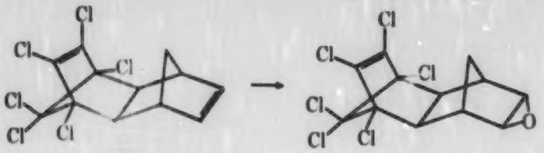
The course of degradation of DDT (1) in soils is not fully established. Certain organisms possess the ability to dehydrohalogenate DDT to DDE (2): Resistant strains of insects are capable of effecting this conversion which is also brought about easily by base or catalytically by iron. Many microorganisms present in soil are capable of converting DDT to DDD (3) under anaerobic conditions. DDD is an important product of DDT degradation (14), but it has proved difficult to ascertain the route of further breakdown after initial conversion to DDD. The production of "polar material" which cannot be recovered from soils has been noted. The anaerobic breakdown of DDT by *Enterobacter aerogenes* microorganisms is reported to yield reduced dechlorinated compounds as well as oxidized derivatives and ultimately *p,p'*-dichlorobenzophenone (4) (15).



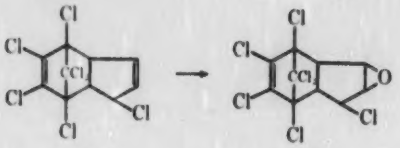


Irradiation of a solution of DDT in methanol or ethanol affords a mixture of compounds. A number of these have been isolated and characterized: DDD is formed by reductive dechlorination, DDE by dehydrochlorination, and *p,p'*-dichlorobenzophenone by oxidation. Also, 2,3-dichloro-1,1,4,4-tetrakis(*p*-chlorophenyl)-2-butene (5) has been isolated from solution (16). Solid DDT decomposes in sunlight and air in a similar manner but the rate of reaction is slower.

Cyclodienes. Aldrin (6) is oxidized to dieldrin (7) and heptachlor (8) to heptachlor epoxide (9) in soils (3). Both epoxides are insecticidal and prolong the biological activity (Fig. 2). Epoxidation is probably mediated by soil microorganisms.

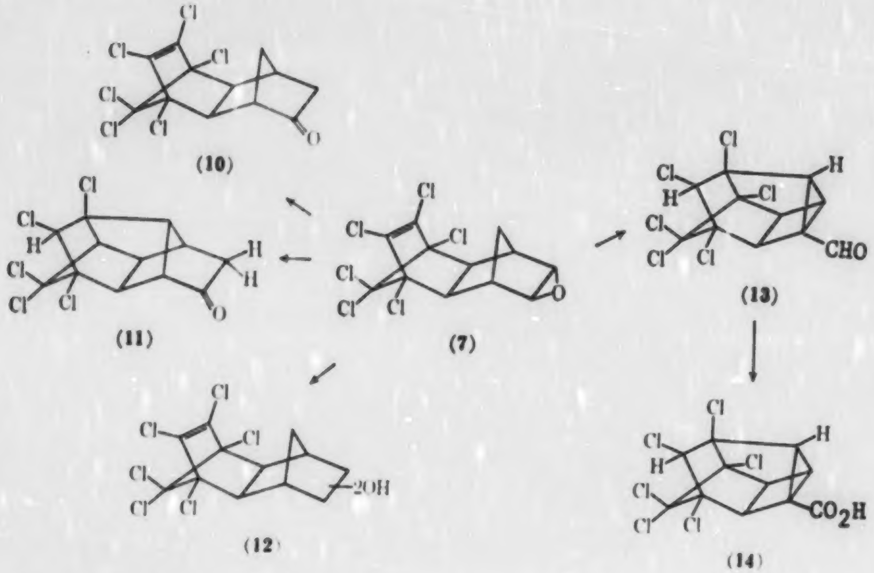


(6) (7)



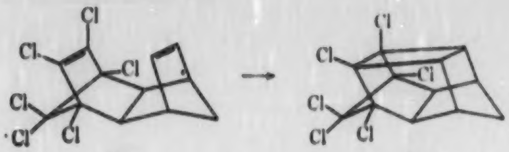
(8) (9)

Dieldrin is degraded by a number of soil microorganisms. The major degradation products resulting from metabolism by *Pseudomonas* spp have been isolated and identified (17). The metabolic products were established for the microorganism and from the soil:

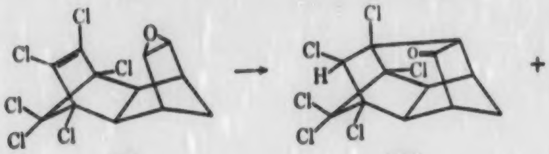


The major metabolites reported were aldrin, a ketone derived by rearrangement of the epoxide ring to a carbonyl function (**10**); a compound (**11**) formed by ring closure in (**10**); probably dihydroxydihydroaldrin (**12**); and, tentatively, an aldehyde (**13**) and an acid (**14**) formed by loss of carbon from the ring to which the epoxide function was formerly attached. *Enterobacter aerogenes* in a culture medium produces 6,7-*trans*-dihydroxydihydroaldrin, which is compound (**12**) with hydroxyl groups at the 6 and 7 positions in the trans orientation, aerobically from dieldrin (18).

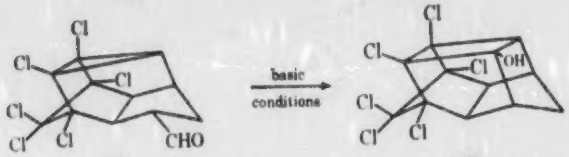
The stereoisomeric chlorinated hydrocarbons, isodrin (**15**) and aldrin, and their corresponding epoxides, endrin (**16**) and dieldrin, undergo a number of reactions when irradiated with ultraviolet rays or natural sunlight (19–22). The yields and products, (**17**) to (**24**), vary with the wavelength of the light, the irradiation period, and the physical state of the irradiated material.


Cl
Cl
Cl
Cl
Cl
Cl
Cl
Cl
Cl
Cl
Cl
Cl

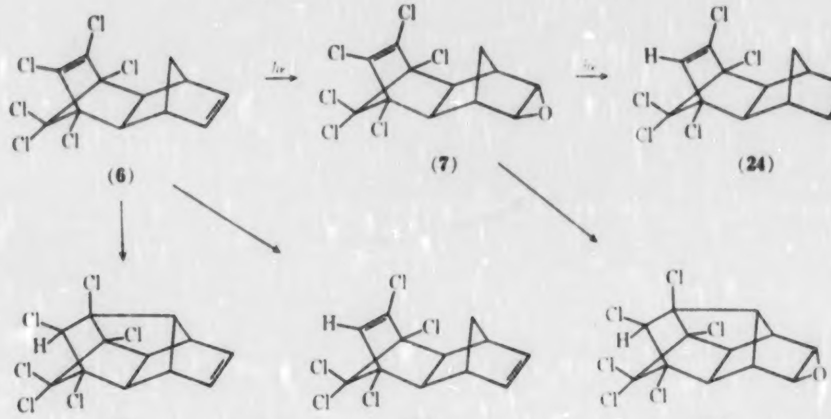
(**15**) (**17**)


Cl
Cl
Cl
Cl
Cl
Cl
O
Cl
Cl
H
O
Cl
Cl
Cl
Cl
+

(**16**) (**18**)


Cl
Cl
Cl
Cl
Cl
Cl
CHO
basic
conditions
Cl
Cl
Cl
OH
Cl
Cl
Cl

(**19**) (**20**)


Cl
Cl
Cl
Cl
Cl
Cl
(6)
hν
Cl
Cl
Cl
Cl
Cl
Cl
O
(7)
hν
Cl
H
Cl
Cl
Cl
Cl
O
(24)
Cl
Cl
H
Cl
Cl
Cl
Cl
Cl
H
Cl
Cl
Cl
Cl
Cl
Cl
H
Cl
Cl
Cl
Cl
O

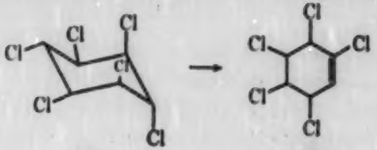
(**21**) (**22**) (**23**)

Isomerization occurs in the solid state to give structures in which an adjacent carbon atom has added to the halogenated double bond. In the process of photoisomerization of endrin, in addition to carbon–carbon bond formation, the epoxide ring rearranges to afford a ketone (**18**).

In dilute solution, one chlorine substituent from the carbon–carbon double bond of dieldrin or aldrin is replaced by a hydrogen atom. Photoexcitation is followed by hydrogen abstraction from the solvent.

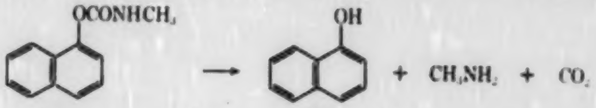
Other photolysis products have been reported: For example, solid aldrin, on exposure to natural sunlight, yields dieldrin and the corresponding photolysis product of dieldrin (**23**) in addition to (**21**). Polymeric material forms the major portion of the photolysate.

Lindane (γ-hexachlorocyclohexane). Lindane (**25**) is less persistent in soil than DDT or the chlorinated cyclodiene insecticides. The degradation product of lindane in soils has been identified by cochromatography as γ-pentachlorocyclohexene (**26**). The evidence supports the view that this may be a microbial conversion (23).



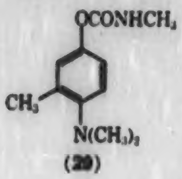
(**25**) (**26**)

Carbamates. Several methyl carbamates are sold as broad-spectrum insecticides. Of these carbaryl (**27**) is the most extensively used. Unfortunately, very little published literature exists on the fate of these insecticides in soils. This scarcity of information probably relates to the short effective life of these compounds. Carbaryl, for example, has a half-life of about eight days in soils. Chemical hydrolysis is probably responsible for the rapid disappearance of carbaryl. Degradation generally involves an initial hydrolysis of the ester linkage. Most methyl carbamates are unstable in alkaline media and consequently localized areas of high pH in soils may facilitate hydrolysis. The products of hydrolysis may then be further degraded. Starting with carbaryl, the products of hydrolysis are 1-naphthol (**28**), methylamine, and carbon dioxide. Methyl isocyanate is a possible transient intermediate.



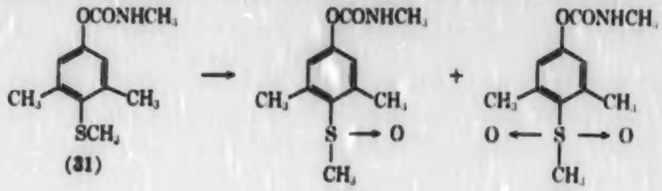
(**27**) (**28**)

Since there is no direct evidence for methyl carbamate metabolism by soil microorganisms, one can only speculate as to probable sites of attack from a study of related systems. Possible points of metabolic attack include hydrolysis of the ester linkage, oxidation of the *N*-methyl group, ring substitution, and ring cleavage. Based largely on the rapidity with which carbaryl breaks down in soils, esterase activity is the favored mode of degradation. The other reactions are generally slower in most soils. Due to their lack of persistence, methyl carbamate insecticides are seldom, if ever, detected in the national soils-monitoring program. A number of carbamate insecticides decompose in sunlight, affording several products (24–26). Carbaryl, Baygon,


OCONHCH$_3$
CH$_3$
N(CH$_3$)$_2$

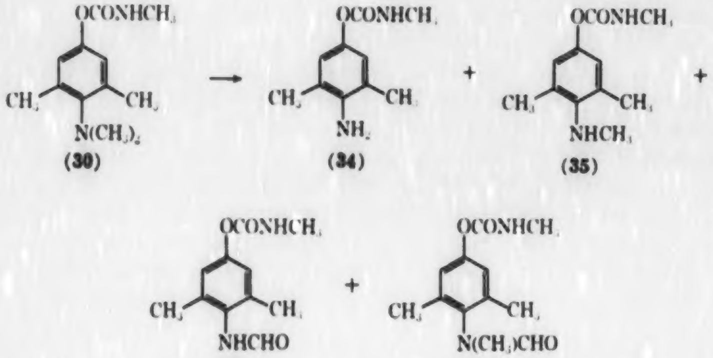
(29)

Banol, Matacil (29), Zectran (30), and Mesurol (31) are subject to photolysis. The major products from Mesurol are the sulfoxide (32) and the sulfone (33):


OCONHCH$_3$
CH$_3$
CH$_3$
SCH$_3$
OCONHCH$_3$
CH$_3$
CH$_3$
S → O
CH$_3$
+
OCONHCH$_3$
CH$_3$
CH$_3$
O ← S → O
CH$_3$

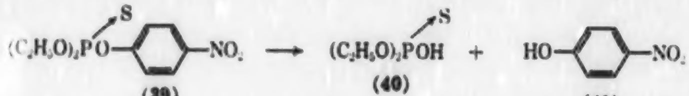
(31) (32) (33)

Matacil and Zectran undergo photooxidation. For example, the dimethylamino group of Zectran is oxidatively dealkylated to the amino (34), methylamino (35), formamido (36), and methylformamido (37) analogs. Matacil behaves in a similar manner. This reaction represents the major pathway of photodecomposition for these compounds.

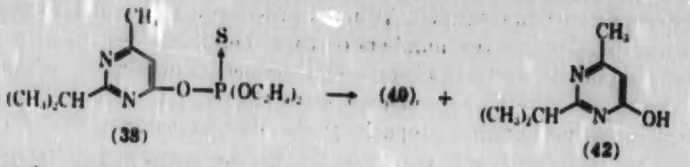

OCONHCH$_3$
CH$_3$
CH$_3$
N(CH$_3$)$_2$
OCONHCH$_3$
CH$_3$
CH$_3$
NH$_2$
+
OCONHCH$_3$
CH$_3$
CH$_3$
NHCH$_3$
+
OCONHCH$_3$
CH$_3$
CH$_3$
NHCHO
+
OCONHCH$_3$
CH$_3$
CH$_3$
N(CH$_3$)CHO

(30) (34) (35) (36) (37)

Phosphates. Like the carbamates, the organic phosphates are cholinesterase inhibitors. Diazinon (38), parathion (39), and phorate are used to control soil-borne insects. The organophosphorus compounds are degraded fairly rapidly. The rate increases with soil moisture. Increase of soil pH favors hydrolysis. The products of hydrolysis of parathion are *O,O*-diethyl phosphorothioate (40) and *p*-nitrophenol (41). Hydrolysis of diazinon yields (40) and 6-hydroxy-2-isopropyl-4-methylpyrimidine (42):


S
(C$_2$H$_5$O)$_2$PO
NO$_2$
S
(C$_2$H$_5$O)$_2$POH
+
HO
NO$_2$

(39) (40) (41)

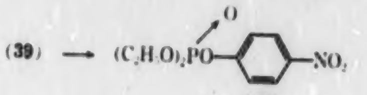

(38) (40) (42)

The process is catalyzed by adsorption and occurs at degradation rates up to 11% per day. Thus chemical hydrolysis may occur so rapidly as to preclude any extensive biological breakdown, especially at low pH values. Diazinon and related pesticides are also readily hydrolyzed in the presence of Cu^{2+} at pH 5–6.

Soil microorganisms have also been implicated in phosphate insecticide degradation. From a comparison of autoclaved and nonautoclaved soil, parathion breakdown was suggested to be influenced by the number and metabolic activity of soil microbes. Malathion was found to be rapidly metabolized by a soil fungus, *Trichoderma viride*, and a bacterium *Pseudomonas* sp isolated from soils receiving heavy applications of the insecticide (25a). *Pseudomonas fluorescens* and *Thiobacillus thiooxidans* metabolize phorate and other phosphorothioates.

It is still unclear as to the respective roles of soil microorganisms vs adsorption in the overall disappearance of organophosphate insecticides in soils. Several suspected microbial systems were reported to attack specific phosphate insecticides. Subsequently, the initial chemical hydrolysis of the phosphate linkage was shown to be followed by metabolism of the resultant products. Autoclaving not only reduces the microbial population, but also substantially alters the structure of many organic components in soils. Consequently, steam sterilization is not always a reliable indicator of microbial involvement, particularly if the initial reaction involves the participation of some labile organic compound in soils. For example, malathion and several other phosphate insecticides decomposed much faster in gamma-radiation-sterilized soils than in autoclaved soils. A heat-labile, water-soluble substance that accelerated malathion degradation has been extracted from several nonautoclaved and radiation-sterilized soils (25b). This substance was destroyed by heating soil suspensions for 10 min at 90°C, but remained stable at room temperatures. Thus, a third component, soil organic matter, appears to be important in phosphate degradation. The finding of a specific organic catalyst for this class of pesticides illustrates an important concept in the soil chemistry of pesticides, ie, the participation of purely organic reactions in soils not mediated by soil microorganisms. The inhomogeneity of soil organic matter, however, has made an understanding of such reactions difficult.

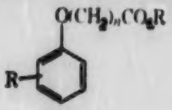
Oxidation of parathion increases the anticholinesterase activity of this insecticide. Thus paraoxon (**43**) is more toxic than the parent compound (26).


(39) (43)

Herbicides

From a research standpoint, the herbicides have been studied more extensively in soils than all other classes of pesticides. Many herbicides are active only when applied to soils. Secondly, and probably more importantly, residual herbicides can damage sensitive crops grown in rotation. As noted previously, about 125 herbicides are marketed commercially. Large numbers of these herbicides belong to a few chemical classes of compounds, each exhibiting similar properties in soils. The important chemical classes include the *phenoxyalkanoic acids* (2,4-D, 2,4,5-T, 2,4-DB, MCPA); the *s-triazines* (simazine, atrazine, propazine); the *phenylcarbamates* (IPC, CIPC, barban); the *chlorinated aliphatic acids* (dalapon, TCA); the *phenylureas* (fenuron, monuron, diuron); the *dinitrobenzenes* (DNBP, trifluralin, benefin); the *benzoic acids* (amiben, 2,3,6-TBA); the *dipyridyls* (paraquat, diquat); and the *thiocarbamates* (EPTC, vernolate). Within these nine classes are found the majority of the important herbicides. Certain herbicides, such as amitrole, are often considered as separate entities. A number of reviews cover the chemistry of herbicides in soils (28–30). Detailed discussions of reactions considered in the following sections will be found in these articles.

Phenoxyalkanoic Acids. The phenoxyalkanoic acids constitute the major single group of herbicides now used in the United States. Production of 2,4-D, 2,4,5-T, and their esters and salts accounted for 32% of the total herbicide production in 1967 (31). The phenoxy herbicides are related by the following common structure:



(44)

Microbial metabolism is the principal mechanism of phenoxyalkanoic acid breakdown within soils. As indicated in Figure 4, loss of 2,4-D occurs more quickly than the

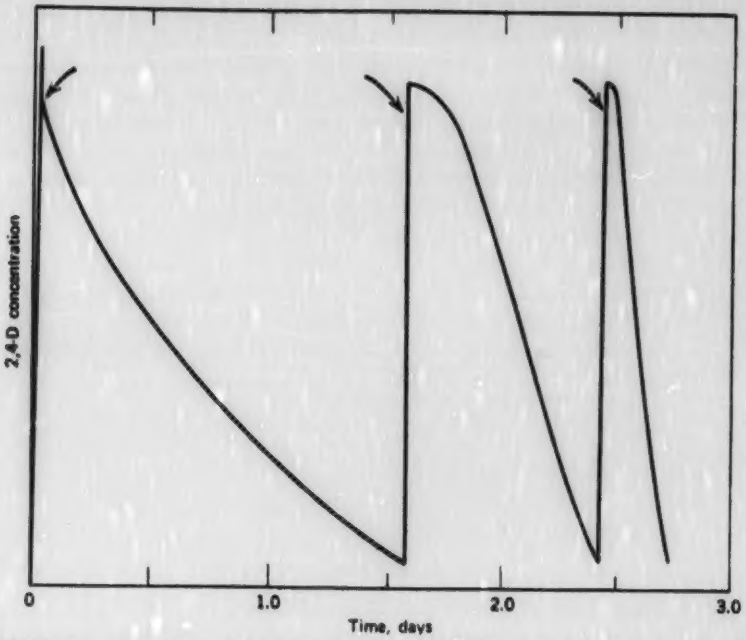
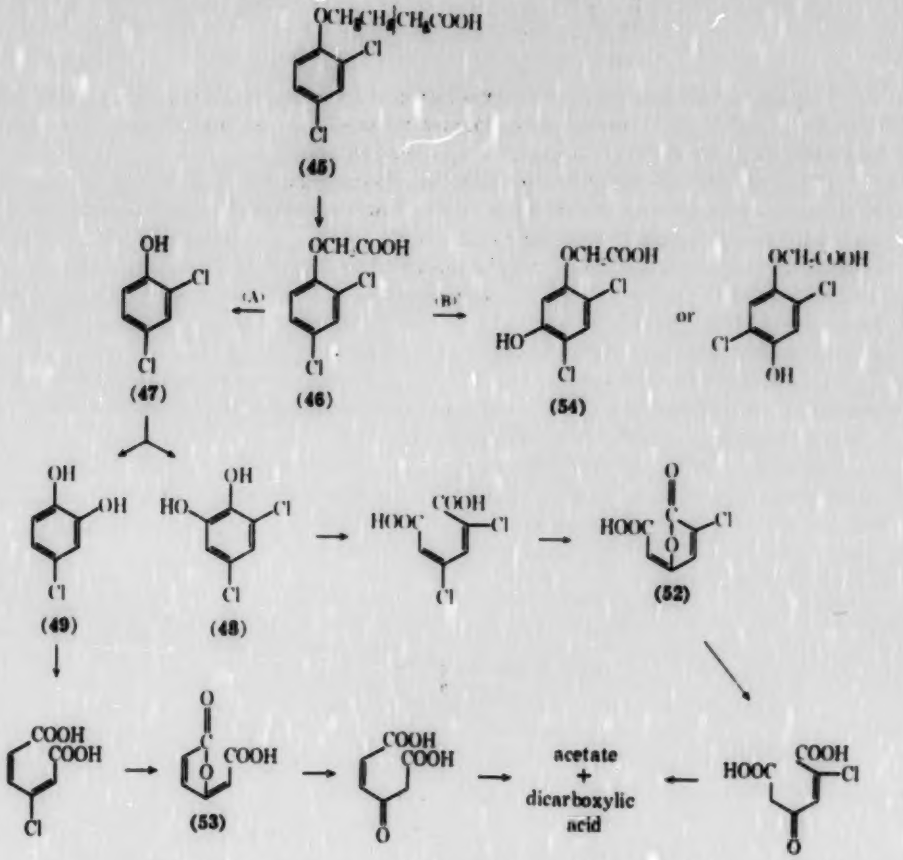


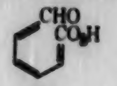
Fig. 4. Metabolism of 2,4-D by soil microorganisms. Degradation occurs more rapidly after each addition of 2,4-D (indicated by arrows.) Adapted from (32).

loss of either MCPA or 2,4,5-T, which is perhaps the most persistent phenoxy herbicide. Warm, moist, and well-aerated soil with ample organic matter favors the growth of microorganisms known to degrade the phenoxides; herbicide persistence can be expected to be fairly short in this environment. The rate of breakdown may also depend on the development of an adaptive population. Repeated increments of 2,4-D (Fig. 4) build up a microbial population which utilizes the herbicide as a carbon source; persistence, after each addition, becomes progressively shorter. An interesting corollary of this is the ability of MCPA-enriched soils to degrade other phenoxyacetic acids, sometimes faster than soils enriched in the test herbicides.

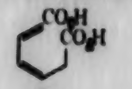
The two major routes of phenoxyalkanoic acid metabolism in soils appear to be (A) initial attack and removal of the aliphatic side chain, followed by alteration of the aromatic ring, and (B) direct hydroxylation of the benzene moiety, often with product accumulation.


OCH₂CH₂CH₂COOH
Cl
Cl
(45)
OH
Cl
Cl
(47)
(A)
OCH₂COOH
Cl
Cl
(46)
(B)
OCH₂COOH
Cl
HO
Cl
(54)
or
OCH₂COOH
Cl
Cl
OH
OH
OH
Cl
(49)
OH
HO
Cl
Cl
(48)
COOH
HOOC
Cl
Cl
O
C
HOOC
O
Cl
(52)
COOH
COOH
Cl
O
C
O
COOH
(53)
COOH
COOH
O
acetate
+
dicarboxylic
acid
COOH
HOOC
Cl
O

Pathway (A) may involve β-oxidation, ie, progressive cleavage of two-carbon fragments along the aliphatic chain. Thus, 2,4-DB (**45**) is converted in soil to its two-carbon analog, 2,4-D (**46**), perhaps via a crotonic acid intermediate. By another mechanism , a *Flavobacterium* sp cleaves the ether bond in a 2,4-dichlorophenoxyalkanoic acid directly, with formation of 2,4-dichlorophenol (47) and the fatty acid. The common metabolite in pathway (A) is the substituted phenol. Ring hydroxylation, a well-known mode of biological detoxication, apparently occurs next. In cultures and enzyme preparations of the soil-isolated bacterium *Arthrobacter* sp, 2,4-D is first converted to 2,4-dichlorophenol, then to 3,5-dichlorocatechol (48). By an analogous process, MCPA is cleaved to 4-chloro-2-methylphenol, then to an unidentified catechol. All steps require molecular oxygen. Other organisms may release chlorine during hydroxylation, affording 4-chlorocatechol (49) from 2,4-D. Cleavage of catechols may occur either adjacent to a hydroxyl, yielding a muconic semialdehyde (50), or between the hydroxyl, with formation of a muconic acid (51). Only muconic acids have thus far been isolated from cultures containing the phenoxy herbicides.



(50)



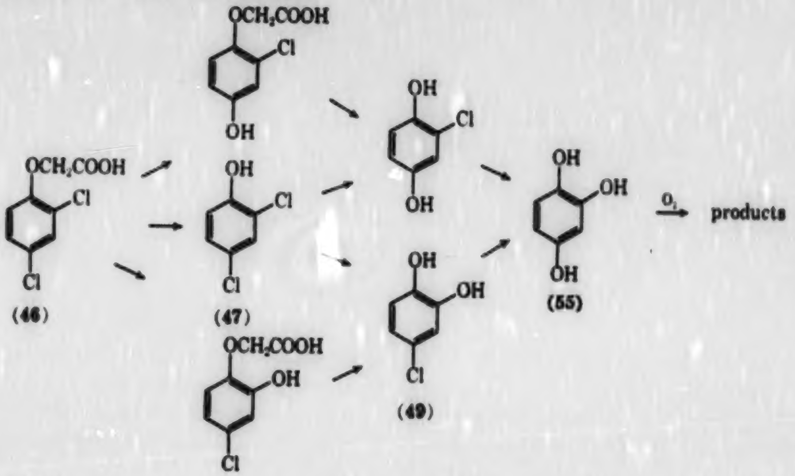
(51)

Further metabolism may proceed via lactone formation, eg (52) and (53) (observed with 2,4-D and MCPA), including loss of any carbon-4 halogen, and ultimate oxidation to carbon dioxide and, in chlorinated compounds, chloride.

Pathway (B), the second major route of phenoxyalkanoic acid metabolism, proceeds by hydroxylation of the aromatic ring. However, β-oxidation to a phenoxyacetic acid may occur initially. The fungus *Aspergillus niger* produces *ortho-* and *para-*hydroxylated phenoxyalkanoates from the unsubstituted acids; the same organism forms 5-OH-2,4-D (54) and 5-OH-MCPA as major products of 2,4-D and MCPA. The formation of 6-hydroxy intermediates by certain bacteria has been postulated; subsequent ether cleavage would yield catechols directly.

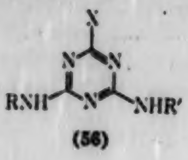
The relative importance in soils of the alternate metabolic pathways whereby phenoxies are degraded is unclear. Soil conditions which govern distribution of microbial populations may be the most influential factors.

The phenoxyalkanoic acids decompose in aqueous solution in sunlight. The major reactions occurring are the fission of the ether bond and sequential replacement of the halogen atoms by hydroxyl groups:



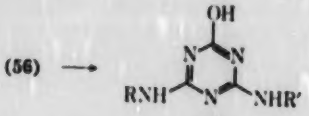
A trihydroxybenzene (**55**) is the ultimate photolysis product but this is susceptible to oxidation in air and can only be isolated (as the acetate) when an oxidation inhibitor such as sodium bisulfite is added to the reaction mixture. Oxidation of trihydroxyphenol by air gives dark-colored polymeric material resembling humic acid.

***s*-Triazines.** The *s*-triazines are primarily used for weed control in corn. Structurally, herbicidal *s*-triazines are generally 2-substituted derivatives of the 4,6-bis-(alkylamino)-*s*-triazines (**56**), where X may be —Cl, —SCH_3, or —OCH_3, and R, R′ are alkyl groups.



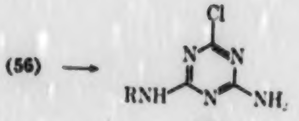
(56)

With a few exceptions, the *s*-triazine herbicides are considered to be immobile, nonvolatile, and unaltered in solution by sunlight. Simazine adsorbed on filter paper is inactivated by sunlight. Chemical and, to a lesser extent, biological reactions play an important role in altering these herbicides in soils. The principal degradation product is the corresponding 2-hydroxy-4,6-bis(alkylamino)-*s*-triazine (**57**). The dehalogenation reaction, in this case, is a chemical reaction facilitated by protonation at the surface of a clay colloid.



(57)

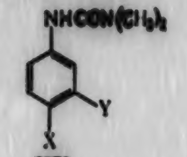
Certain soil fungi (*Aspergillus fumigatus*, *Rhizopus stolonifer*, and *Penicillium decumbens*) can dealkylate the side chain groups to produce the corresponding 2-chloro-4-amino-6-alkylamino-*s*-triazines (**58**).



(58)

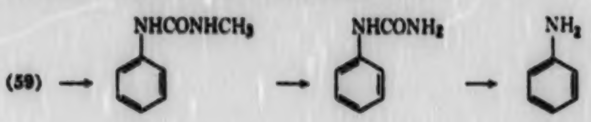
Detailed radioactivity studies with alkyl-^{14}C- and ring-^{14}C-labeled *s*-triazine herbicides indicate that chemical reactions are primarily responsible for degrading the herbicidal 2-chloro-*s*-triazines in most soils.

Phenylureas. Phenylurea derivatives find wide application as herbicides, particularly in cotton growing. Most members of this family possess the 1,1-dimethyl-3-phenylurea moiety (**59**) as part of their structure, where X and Y may be various substituents, such as —H, —Cl, —CF_3, and —OC_6H_5. A few of the phenylureas are 1-methoxy 1-methyl substituted compounds.



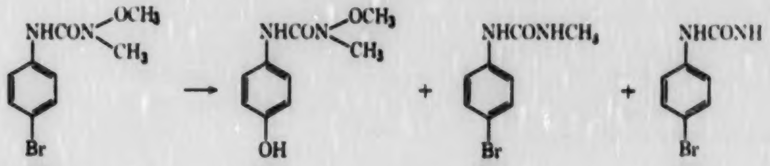
(59)

In soils, the phenylureas behave somewhat like the *s*-triazines, being relatively immobile and nonvolatile. Degradation occurs under conditions most conducive for microbial activity, ie, warm, moist soils with high organic matter content. Although the causative organisms are difficult to isolate, the following pathway has been proposed for the degradation of the phenylurea herbicides in soil:



All of the corresponding products in the above pathway have been detected from the herbicides monuron, diuron, and chloroxuron. *N*-Dealkylation is a reaction common to many pesticides and is apparently mediated by mixed-function oxidase systems requiring molecular oxygen.

Urea herbicides readily undergo photolysis. Metabromuron (**60**), a representative urea herbicide, decomposes in aqueous solution on exposure to sunlight (33). The major product is 3-(*p*-hydroxyphenyl)-1-methoxy-1-methylurea (**61**). Present in lesser amounts are 3-(*p*-bromophenyl)-1-methylurea (**62**) and *p*-bromophenylurea (**63**). Substituted diphenyl derivatives may also be formed.

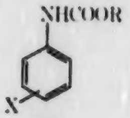


(60) (61) (62) (63)

Chloroxuron decomposes on irradiation and degrades by sequential loss of *N*-methyl groups. Monuron, neburon, diuron, linuron, and fenuron are also degraded by sunlight.

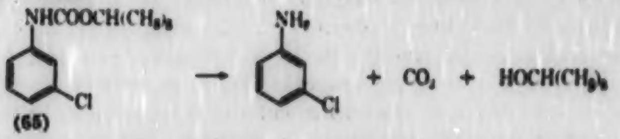
Phenylcarbamates. The phenylcarbamate herbicides differ considerably from the methylcarbamate insecticides in soils. The herbicidal carbamates are lost from soils by volatilization and metabolism by soil microorganisms.

This group has as its primary structure a phenylcarbamic acid esterified with various alcohols (**64**).



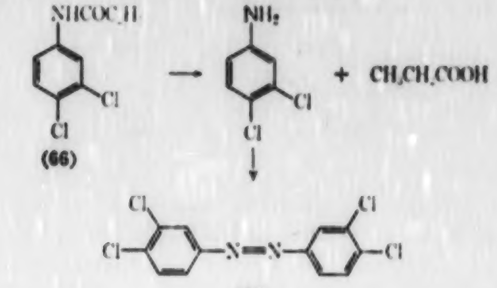
(64)

Microorganisms (***Pseudomonas striata*, *Flavobacterium*, *Azobacterium*, and *Achromobacter***) metabolize these herbicides to an aniline, an alcohol, and carbon dioxide, as shown with CIPC (**65**).


NHCOOCH(CH3)2
Cl
NH2
Cl
+ CO2 + HOCH(CH3)2

(65)

The acylanilides are also aniline-based herbicides closely resembling the phenylcarbamates. An important member of this group is propanil (**66**), the principal herbicide used for weed control in rice. Soil microorganisms cleave propanil to yield 3,4-dichloroaniline and propionic acid. The dichloroaniline undergoes a condensation reaction to form the 3,3′, 4,4′-tetrachloroazobenzene (**67**).

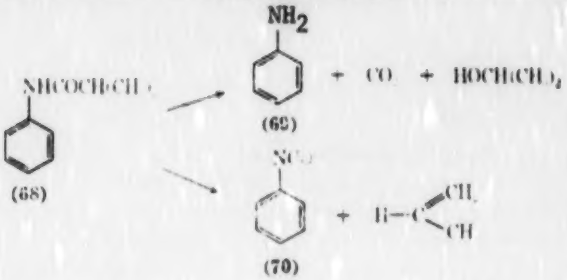

NHCOC2H5
Cl
Cl
NH2
Cl
Cl
+ CH3CH2COOH
Cl
Cl
N=N
Cl
Cl

(66)

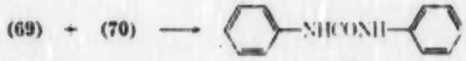
(67)

Azobenzenes have also arisen from several other chlorosubstituted anilines when incorporated in soils.

The carbamate herbicide IPC (**68**) photodecomposes by at least two pathways.


NHCOCH(CH3)2
NH2
+ CO2 + HOCH(CH3)2
NCO
+ H—C
CH3
CH3

(68) (69) (70)


(69) + (70)
NHCONH

(71)

Reaction of the aniline (**69**) and phenyl isocyanate (**70**) yields *sym*-diphenylurea (**71**).

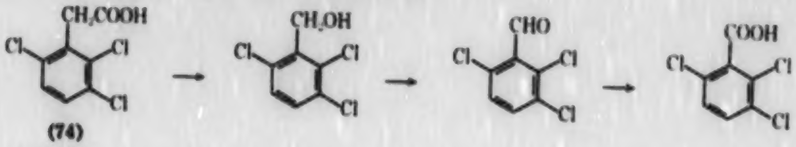
Chlorinated Alkyl and Aryl Acids. Two chlorinated aliphatic acids, TCA (**72**) and dalapon (**73**), are used extensively as herbicides.

CCl_3COOH (**72**)

CH_3CCl_2COOH (**73**)

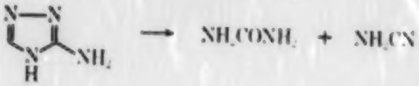
Microorganisms rapidly metabolize most members of this family of herbicides by replacing the halogen to form the corresponding hydroxy or keto acids. For example, dalapon yields pyruvic acid via enzymic hydrolysis by a system isolated from an *Arthrobacter* sp. Little is known about the metabolism of the chlorinated aromatic acids. Replacement of chlorine by the hydroxyl group commonly occurs when an aqueous solution of a chlorinated aromatic acid is exposed to sunlight. Reductive dehalogenation may also take place when chlorine is replaced by hydrogen; however, this reaction is more favored in hydrogen donor solvents such as cyclohexane.

Loss of chlorine from the ring is preferred in certain orientations: Amiben, 3-amino-2,5-dichlorobenzoic acid, loses the chlorine atom preferentially from the 2 position. A chlorine atom which is substituted meta to a carboxylic acid group is more resistant to photolysis than an ortho or para chlorine substituent. In addition, chlorinated phenylacetic acids also undergo reaction in the side chain and the probable sequence of reactions is indicated with fenac (74).



(74)

Amitrole. Amitrole gained national prominence in 1960 when residues of this herbicide were detected in cranberries. Metabolic studies with amitrole have been conducted in plants, where several adducts have been isolated and identified. The fate of amitrole (75) in soil is governed principally by the activity of soil microorganisms, adsorption on soil colloids, and chemical transformations. Free radicals, derived from microbial or chemical processes in soils, probably play an important role in amitrole degradation. A number of model free-radical-generating systems yield the following products:

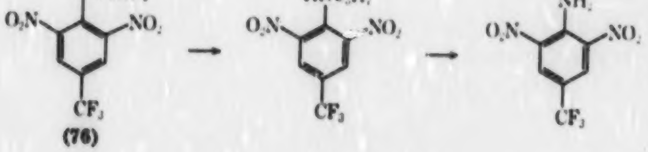


(75)

Similar systems are probably responsible for amitrole degradation in soils.

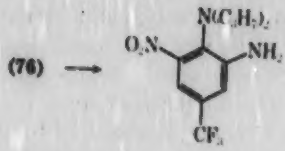
Amitrole degradation by ultraviolet irradiation affords the same products that are obtained by riboflavin-sensitized photolysis at the wavelengths of visible light. Urea and cyanamide can be obtained from the reaction mixture; the photolysis parallels the reaction of amitrole with hydroxyl radicals generated by Fenton's reagent (34).

Dinitroanilines. Trifluralin (76), nitralin, and bensulide are relatively new herbicides used in cotton and soybean cultivation. Photodecomposition, volatility, and soil microorganisms contribute to the disappearance of these herbicides. Degradation proceeds by sequential removal of the *N*-alkyl groups as shown with trifluralin:



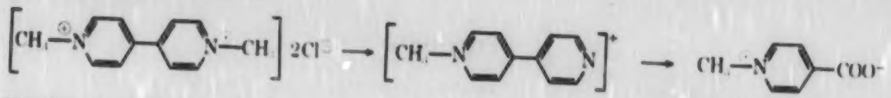
(76)

Under anaerobic field conditions, ie, in flooded soils, the nitro group in trifluralin is reduced to an amino group.

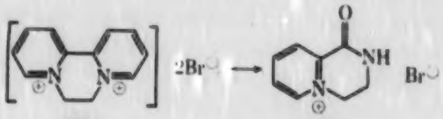


Combinations of these two pathways occur in certain soils.

Dipyridyls. The organic cations, paraquat (77) and the closely related diquat (78), are desiccants and aquatic herbicides. In soils, they are tightly adsorbed by cation exchange to some soil particles and, consequently, inactivated almost immediately. In soil enrichment cultures, however, bacteria have been isolated which carry out the following series of reactions:



Similar degradation products of paraquat have been identified in photochemical studies. Diquat decomposes in sunlight and affords a tetrahydropyridopyrazidinium salt (79) as a major product.



(78) (79)

Arsenical Pesticides

Inorganic arsenicals, such as arsenic trioxide, As_2O_3; arsenic pentoxide, As_2O_5; sodium arsenate, Na_2HAsO_4; sodium arsenite, nominally Na_3AsO_3; lead arsenate, $Pb_3(AsO_4)_2$; calcium arsenate, $Ca_3(AsO_4)_2$; and Paris green, $3Cu(AsO_2)_2 \cdot Cu(C_2H_3O_2)_2$, have been used in agriculture for many years as insecticides, herbicides, soil sterilants, and silvicides. Arsenic is ubiquitous in nature and occurs naturally in soils; the average content in soils collected from various countries is about 5 ppm. Quantities ranging from a trace to 14 ppm have been reported for most soils.

The continued use of arsenic pesticides in early pest control programs has increased the residual content in certain soils. For example, arsenic residues of 440 ppm have been reported in orchard soils with a history of lead arsenate applications. Beans exhibit toxic symptoms when grown on these soils (35). A more recent survey reports residues of up to 2500 ppm in soils treated with lead arsenate in the 1930s.

The inorganic arsenicals have largely been replaced by the less toxic organic arsenicals. Two important organic arsenicals in use today are DSMA, $CH_3AsO(ONa)_2$, and cacodylic acid, $(CH_3)_2AsO(OH)$. They are considerably less toxic than the inorganic arsenicals; LD_{50} equals 1800 and 830 mg/kg, respectively. DSMA is particularly effective against the perennial weed johnson grass and affords one of the most economical methods of control in areas of heavy infestation. Cacodylic acid is a contact herbicide which will defoliate or desiccate a large variety of plants.

Rice is particularly sensitive to arsenic residues in soils (36). One theory to explain the greater sensitivity of rice to arsenic residues maintains that under waterlogged conditions, soils are in a highly reduced condition and arsenate is reduced to the more toxic arsenite. The toxic trivalent form would seriously impair growth of rice. Another theory maintains that reduction of arsenic to arsine by certain soil fungi could explain the hypersensitivity of rice. The alkylarsines are foul-smelling gases, highly toxic to mammals. Trimethylarsine, $(CH_3)_3As$, is produced by certain strains of molds in the presence of arsenic trioxide or sodium cacodylate (37). It has been suggested that arsenic is lost from soils as an alkyl arsine.

Arsenate residues in soils exist in the following five forms: water-soluble, iron, aluminum, calcium, and nonextractable arsenate. The amount of any one form varies, depending on the amount of cation present. The water-soluble arsenate is the most toxic to plants. The iron and aluminum salts are extremely insoluble and consequently are relatively less phytotoxic.

Fungicides

Fungicides are used at low rates as seed protectants and disinfectants on a major portion of the total crop acreages. On more limited acreages, however, fairly high rates are used to control diseases on citrus, apples, and other deciduous fruits and, to a lesser extent, on other fruits and vegetables (1).

Most fungicides can be conveniently placed in the following classes of compounds: sulfur, copper, mercury, carbamate, imidazoline, quinone, and guanidine. Captan is an important fungicide not readily classified in the above system. Unfortunately, little published literature exists on the fate of many organic fungicides in soils. Several excellent references exist on fungicides (38,39) and their properties in soils (40).

Sulfur and Copper. The inorganic fungicides, including sulfur and Bordeaux mixture, $CuSO_4 + Ca(OH)_2$, are among the oldest known pesticides. Elemental sulfur was first recommended for the control of powdery mildews (*Ershiphaceae*) in 1835 (38). In soils, elemental sulfur is oxidized slowly by chemical means, but rapidly by microbiological reactions. Nonfilamentous, chemoautotrophic bacteria of the genus *Thiobacillus*, heterotrophic bacteria, fungi, and actinomycetes are the principal sulfur oxidizers in soil. The product of microbial oxidation is the sulfate ion, the form in which higher plants absorb practically all of their sulfur.

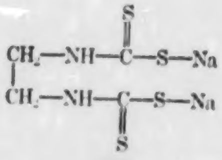
Copper, like arsenic, is a natural component in soils and ranges in concentration from 1 to 50 ppm (41). Organic soils tend to fix copper and hence it does not move from its site of application. In France, for the last sixty years, Bordeaux mixture has been applied annually to vineyard soils at a rate of about 2770 lb of copper sulfate per acre without phytotoxic effects. In the United States, 80 lb per acre of copper sulfate added over thirty-two years to some Long Island potato soils caused no plant injuries.

Mercury. Mercurous chloride, Hg_2Cl_2, and the organic mercurials, including methyl, ethyl, and phenyl mercury derivatives, are used as seed disinfectants. The action of mercurous and mercuric chloride applied to soils results from the release of mercury vapor. Soil factors which increase the reduction of mercury salts to metallic mercury include greater soil moisture and organic matter contents, pH, and temperature.

Metallic mercury and trace amounts of phenylmercury acetate (PMA) were detected in the air surrounding soil following PMA treatment (42). Ethyl mercury acetate treatment afforded approximately equal amounts of mercury vapor and the vapor of the ethylmercury compound. Methylmercury compounds gave methylmercury vapor with a trace quantity of mercury vapor. After 30–50 days a large portion of soil-applied organic mercurial compound was found to be unaltered.

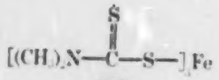
Carbamates. Most commercially available carbamate fungicides are derivatives of dithiocarbamic acid, $NH_2{-}CS_2{-}H$. These derivatives may be classified into the following three groups: thiuram disulfides, $R_2N{-}CS_2{-}CS_2{-}NR_2$; metallic dithiocarbamates, $R_2N{-}CS_2{-}$metal; and ethylenebisdithiocarbamates, $(CH_2{-}NH{-}CS_2)_2{-}$metal.

The nonvolatile fungicides nabam (**80**) and ferbam (**81**) were reported to be inactivated nonbiologically in soils, whereas Semesan (**82**) was metabolized by soil microorganisms. Under similar conditions captan (**83**) was recovered unchanged after 150 days (43).



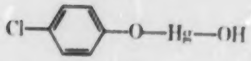
$$\begin{array}{l} \mathrm{CH_2{-}NH{-}\overset{\overset{S}{\|}}{C}{-}S{-}Na} \\ | \\ \mathrm{CH_2{-}NH{-}\underset{\underset{S}{\|}}{C}{-}S{-}Na} \end{array}$$

(**80**)

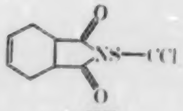


$$\mathrm{[(CH_3)_2N{-}\overset{\overset{S}{\|}}{C}{-}S{-}]_3Fe}$$

(**81**)



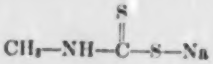
(**82**)



(**83**)

Nabam in soils produces a number of volatile fungitoxic materials, including carbon disulfide; ethylene diisothiocyanate, $(CH_2{-}N{=}C{=}S)_2$; and carbonyl sulfide, CSO (44). In addition, ethylenediamine, $NH_2{-}CH_2{-}CH_2{-}NH_2$; ethylene(thiocarbamoyl)disulfide; and ethylenebis(thiocarbamoyl)monosulfide have been reported as degradation products of ethylenebisdithiocarbamate fungicides (39).

Vapam (**84**) decomposes in soil to the methyl isothiocyanate and *N,N′*-dimethylthiourea. Decomposition is apparently a chemical process favored by increased soil temperature and decreased moisture content. At 40°C and 6% moisture, vapam degradation occurs after 1.5–2.5 hr (45).



$$\mathrm{CH_3{-}NH{-}\overset{\overset{S}{\|}}{C}{-}S{-}Na}$$

(**84**)

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PESTICIDE REGULATION

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Introduction

For the purposes of this summary, the laws and regulations governing pesticides have been divided into two main groups, based upon the source of the law, viz: Federal and State.

Another equally valid division could be made according to what is to be regulated, viz: first, the pesticide chemical itself, its chemistry, toxicity, and labeling; and second, regulation of the person who uses the pesticide. The laws governing the groups resulting from this type of division are the familiar "registration and labeling laws," and the "use and application laws."

Reorganization of Federal Pesticide Control Responsibilities

In discussing Federal pesticide control legislation, mention should be made of Reorganization Plan No. 3, of 1970 (submitted to Congress by President Nixon on July 9, 1970) which established the Environmental Protection Agency (E.P.A.) as a separate organizational unit in the Federal Government, effective December 2, 1970.1/

This reorganization did not produce new pesticide control laws, but it did bring together under one roof, some or all legal functions of certain agencies or departments of the government relating to pesticide control (and other environmentally harmful substances or practices).

The reorganization plan (which has the effect of law) states, in part "...there are hereby transferred to the Administrator (E.P.A.):

> "(1) all functions vested by law in the Secretary of Interior and the Department of Interior which are administered through the Federal Water Quality Administration...
>
> "(2) functions vested in the Secretary of Interior...(relating to studies on the effects of insecticides, herbicides, fungicides, and pesticides upon the fish and wildlife resources of the United States)2/

1/ 35 F.R. 15623

2/ Act of August 1, 1958, 72 Stat 479, 16 U.S.C. 742d-1

> "(4) the functions vested in the Secretary of Health, Education, and Welfare of establishing tolerances for pesticide chemicals under the Federal Food, Drug, and Cosmetics Act...
>
> "(8) (i) The functions of the Secretary of Agriculture under the Federal Insecticide, Fungicide, and Rodenticide Act..."

While each Federal pesticide control law retains its legal identity, the administration of all pesticide laws are now in one agency (some research and related pesticide investigations will still be carried out by other Federal agencies and some agencies have regulations relating, in part, to pesticides).

It should be kept in mind that a pesticide control law may be but a small part of a more comprehensive law relating to a broad subject, or added as an amendment to existing legislation (e.g., The Miller Amendment to the Federal Food, Drug, and Cosmetic Act).

Federal Laws

Federal Insecticide, Fungicide, and Rodenticide Act.[3]

The Federal Insecticide, Fungicide, and Rodenticide Act of 1947 (FIFRA) replaced and expanded the Insecticide Act of 1910.[4] The old act regulated insecticides and fungicides only and at a time when such products were comparatively simple, consisting mainly of Paris green, pyrethrum, bordeaux mixtures, and like products.

The purpose of the law is to regulate the marketing of economic poisons and devices by means of a registration and labeling procedure which requires producers to present evidence of the safety of these products when used as directed and their effectiveness for the purpose claimed on the label.

The Act prohibits shipment in interstate commerce of products which are not registered or are adulterated or misbranded. Products found in violation of the Act may be seized and criminal action instituted against the producer.

In 1959, the Act was amended[5] and updated to include nematocides, plant regulators, defoliants, and desiccants as economic poisons. Poisons and repellents used against amphibians, reptiles, birds, fish, mammals, and invertebrates, are, by regulation, classed as economic poisons.[6]

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[3] 61 Stat. 163; 7 U.S.C. 135 et. seq.

[4] 36 Stat. 335

[5] 73 Stat. 286

[6] 7 C.F.R. 362.2(c)

A 1964 amendment eliminated a controversial "registration under protest" section which had permitted marketing of an unregistered pesticide pending the outcome of full investigation of its usefulness.

Until December 2, 1970, the Act was administered by the Director of the Pesticides Regulation Division, Agricultural Research Service, USDA. The Pesticide Regulation Division also issued interpretations with respect to certain of the more troublesome regulations; e.g., claims for safety and non-toxicity, warning and caution statements, labels for large containers, directions for use, etc.

This law is now administered by the Environmental Protection Agency under the authority of Reorganization Plan No. 3 of 1970.

Federal Food, Drug, and Cosmetic Act of 1938.7/

The Federal Food, Drug, and Cosmetic Act of 1938 (FFDCA) which provides for the regulatory activities of the Food and Drug Administration concerned with foods, drugs, devices, and cosmetics, did not cover pesticides as a separate subject of regulation at the time of its enactment.

In 1954 the FFDCA was amended8/ to require regulation of pesticide chemicals in or on raw agricultural commodities shipped in interstate commerce.

The amendment provides that "any...pesticide chemical...added to a raw agricultural commodity, shall be deemed unsafe...unless--

> "(1) a tolerance for such pesticide chemical...has been prescribed, or
>
> "(2) the pesticide chemical has been exempted from the requirement of a tolerance..."

The amendment also provides that the Secretary of Agriculture shall certify to the Secretary of Health, Education and Welfare that the pesticide chemical is useful for the purpose for which a tolerance or exemption is sought (or that the applicant requesting certification shall be told that the pesticide chemical does not appear to be useful for the intended purpose).

7/ 52 Stat. 1040; 21 U.S.C. 301 et. seq.

8/ 68 Stat. 511; 21 U.S.C. 3462 (Miller Amendment)

Federal Water Pollution Control Act (1948).[9]

Federal Water Pollution Control Act (1948), as amended, relates to pollutants, including pesticides, in water and waterways. It is interesting to note that Federal legislation as early as 1899[10] had made it unlawful to deposit refuse matter of any kind, other than that flowing from streets or sewers in a liquid state, into any navigable waters or its tributaries, unless a permit for such disposal had been obtained from the U.S. Corps of Engineers. The law, mostly dormant since its inception, is now being implemented through a permit system.

Since December 2, 1970, all authorities of the Federal Water Pollution Control Act are administered by the Environmental Protection Agency.

Federal Regulations

Extensive regulations have been issued by the Food and Drug Administration, the Department of Agriculture, and the Federal Water Quality Administration to implement the administration of the three above listed laws.

Additionally, regulations have been issued by other Federal agencies under their basic authorities which relate in part but not exclusively, to pesticides.

Department of Transportation (DOT)

Four agencies of this Department are concerned with and have statutory responsibility for the safe transportation of hazardous materials in interstate commerce.

Within the DOT is a Hazardous Materials Regulation Board which consists of the Administrator(s) of Aviation, Highway, Railroad, Coast Guard, and the Department's Assistant Secretary for Research and Technology.

It is within their authority to promulgate reasonable regulations to assure safety in transporting dangerous articles or substances in interstate and foreign commerce. Additionally these agencies within the DOT may issue regulations of their own which relate to their statutory responsibilities. Pesticides are only one of many such materials and for purposes of regulation most all are included in "Class B" poisons. Regulations are very specific concerning shipping containers, labels, and the handling of pesticides.

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[9] 62 Stat. 1155; 33 U.S.C. 466 et. seq.

[10] 30 Stat. 1152; 33 U.S.C.A. 407

The Federal Aviation Agency has issued regulations[11] relating to agricultural aircraft operations, including tests of pilots regarding their knowledge of dispensing of agricultural materials or chemicals.

Among other things, the test may include:

"(i) steps to be taken before starting operations, including survey of the area to be worked;

"(ii) safe handling of economic poisons and the proper disposal of used containers for those poisons-

"(iii) the general effects of economic poisons and agricultural chemicals on plants, animals, and persons, with emphasis on those normally used in the areas of intended operations; and the precautions to be observed in using poisons and chemicals;

"(iv) primary symptoms of poisoning of persons from economic poisons, the appropriate emergency measures to be taken, and the location of poison control centers..."

Additionally, the holder of a commercial agricultural aircraft operator certificate "shall maintain and keep current, at the home base of operations designated in his application, the following records:

"(1) the name and address of each person for whom agricultural aircraft services were provided;

"(2) the date of the service;

"(3) the name and quantity of the material dispensed for each operation conducted; and

"(4) the name, address, and certificate number of each pilot used in agricultural aircraft operations and the date that pilot met the knowledge and skill requirements of sec. 137.19(e)..." (the test referred to above).

The Federal Trade Commission, organized as an independent administrative agency in 1915, is charged with keeping competition both free and fair. As part of their responsibilities, they regulate the advertising of economic poisons and generally prohibit any advertising which "contradicts, negates, detracts from, or is inconsistent with any statement, warning, or direction for use, in the labeling of such product..."[12]

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[11] 14 C.F.R. 137

[12] 16 C.F.R. 416; 35 F.R. 12727

They have proposed, but not yet adopted, a proposed warning statement for all economic poisons stating "...this product can be injurious to health; read the entire label carefully and use only as directed."

Executive departments and agencies of the Federal Government are required to publish their regulations and the Code of Federal Regulations has been established to accomplish this statutory requirement. The code books are revised as of January 1 each year and kept up to immediate date by daily issues of the Federal Register, in which all new or amended regulations are promulgated. Hence, to find any specific tolerance or exemptions from a tolerance for any particular pesticide in or on a raw agricultural commodity, it would be necessary to look in the current Code of Federal Regulations (Title 21 - Food and Drugs, Chapter 1, Subchapter B, Part 120) and then to check the daily issues of the Federal Register for changes (these contain cumulative indices by both subject matter and sections affected).

State Laws and Regulations

State regulation of pesticides preceded that of the Federal Government by a few years, with New York adopting a law in 1898 which regulated the sale of Paris green. Soon after this, Oregon and Texas (1899) and California, Louisiana, and Washington (1901) passed similar legislation.

State pesticide control laws may be divided arbitrarily into the two following groups:

Registration Laws

Those which regulate the production and marketing of pesticides by requiring compliance with registration and labeling criteria prior to interstate or intrastate shipment. These are often referred to as "economic poison laws" or "insecticide, fungicide, and rodenticide acts."

Following the adoption of the Federal Insecticide, Fungicide, and Rodenticide Act in 1947, many states enacted similar legislation requiring registration and labeling of economic poisons as a prerequisite to their lawful introduction and shipment in commerce. As a result, all except two states now have pesticide registration laws, although not all states have fully implemented the authority granted. Some states exempt pesticides which have been registered under the Federal Insecticide, Fungicide, and Rodenticide Act.

The registration laws which are fully operative are considered "uniform" acts and a comparative study would show little difference in content and objectivity.

The Council of State Governments has developed a model State insecticide, fungicide, and rodenticide act which incorporated the 1959 and 1964 amendments to the Federal Insecticide, Fungicide, and Rodenticide Act, together with suggested regulations for its administration and enforcement.

Use and Application Laws

Those which:

(1) require examination and licensing of persons engaging in the business of applying pesticides (e.g., custom applicators, structural pest control operators, certain sanitation services, equipment operators, etc.),

(2) regulate professions concerned with the use and application of pesticides including consultation services and recommendations for treatment (e.g., entomologists, plant pathologists, horticulturists, tree surgeons, etc.),

(3) (a) prohibit or restrict the use of certain pesticides,

(b) require (i) the purchaser to obtain a permit before using highly toxic pesticides (usually a written "prescription") giving the kind of pesticide to use, the concentration permitted, the crop to be treated, method of application, and precautions to be observed, and (ii) dealers in "prescription" pesticides to be licensed.

Of the various categories of State pesticide use and application laws, probably the structural pest control laws are the most uniform, and those which relate to the use and application of agricultural pesticides, the least uniform. Unfortunately, the "model" use and application acts prepared by concerned groups have followed, rather than preceded, enactment of legislation in this field.

Use and application laws generally establish qualifications for applicants; they may require both oral and written examinations; establish fees; provide for issuance, renewal, and cancellation of licenses; and grant reciprocity to nonresidents meeting standards equal to those of the licensing state.

Applicators are required to be financially responsible for the consequences of their acts and, to this end, a liability insurance policy or its equivalent, is a prerequisite to issuance of a license.

In the model "custom application of pesticides act" prepared by the Association of American Pesticide Control Officials and published in the

1971 program of Suggested State Legislation by the Council of State Governments and in a similar model of the Food and Drug Administration, the Commissioner of Agriculture, Pesticide Control Board, or other official responsible for administration of the law, is generally given statutory authority to:

1. issue regulations
2. enforce the act
3. delegate duties
4. prescribe, restrict, or prohibit methods or materials
5. inspect premises
6. inspect equipment
7. require records or reports
8. cooperate with other agencies
9. publish information
10. conduct training courses
11. regulate storage, transportation, or disposal of pesticides or pesticide containers
12. require compliance with label directions
13. license equipment
14. subpoena persons or records
15. require filing reports of loss
16. investigate damages

Provision is made for a pesticides board in order to give representation to all groups who have a legitimate interest in controlling the use and application of pesticides. In the past, some boards have been of an advisory nature only, but more recent legislation grants the boards considerable regulatory authority, including the power to either issue rules and regulations governing pesticide use and application, or to approve them before they become effective.

Twenty states have pesticide boards, but the authority, membership, and representation vary considerably from state to state.

The use and application laws have generally exempted individuals and governmental bodies who apply pesticides for their own use; however, recent legislation indicates a trend to reduce such exemptions.

As indicated, most pesticide control laws have been classified as either "registration" or "use and application" laws; however, within the last 2 or 3 years, some "registration" laws have been amended to include sections on "use and application" of pesticides.

In Florida and a number of other states, such amendments have been made which restrict the use of certain pesticides. These restricted use pesticide laws generally authorize the Commissioner of Agriculture, or some governmental body, to determine which pesticides should be restricted in their use and to establish procedures regulating their purchase and application. The most common method of control is to require any person desiring to use a pesticide on the restricted list, to obtain a permit from a state or county official knowledgeable in the subject. The permit specifies the pesticide to be used, the crop to be treated, etc. Such pesticides may be sold only by a dealer licensed by the state to deal in such chemicals, and who may sell only to a person presenting a valid permit.

Alaska's 1970 pesticide law is a single act which relates to"... transporting, testing, inspecting, packaging, labeling, handling... advertising...and use of pesticides."

State pesticide laws governing tolerances for pesticide residues in or on raw agricultural commodities generally follow Sec. 408 of the Federal Food, Drug, and Cosmetic Act (Miller Amendment).

It should be kept in mind that a large part of pesticide control is accomplished by regulations issued under authority of the appropriate law; e.g., the Michigan custom applicator's law states, "...the director may promulgate rules to carry out the provisions of this act...," and under this authority very specific details are issued regulating the use and application of pesticides.

Ordinances

A few local governmental bodies and municipalities have adopted ordinances and regulations which, in part, control the use of pesticides. Perhaps the most common are those which prohibit or restrict the use of highly toxic rodenticides or other pesticides by pest control operators in homes, warehouses, and structures. Some of the earliest local legislation related to fumigation practices in residences, ships, warehouses, etc.

The considerable amount of State and Federal legislation regulating pesticides has reduced the need for local ordinances; however, in the 15 states without use and application laws and in the two states without registration laws, local ordinances would be necessary if control of pesticides is to be accomplished.

Pesticides in Food

Dale R. Lindsay, Ph.D.

It is impossible to deal with this subject without infringing on the topics of other speakers, but I shall attempt to minimize the intrusion. To get some of these overlapping topics out of the way, let me begin by pointing out the obvious ones in the order of appearance of the speakers.

Dr. Lichenstein will already have told you a good deal about pesticides in food (incidentally, water is a food) and the significance to man of the chemicals or their metabolites. The chemistry and physics are extremely important to detecting pesticides in foods as well as the affinity of pesticides for foods. The results of these tests are used in regulations. We are concerned primarily with pesticides in foods because of their hazard to man. I've already mentioned that water is a food. There is considerable evidence that much food contamination with pesticides is from air. Changing pesticide patterns have a direct bearing on all of the above. The remaining six topics obviously are similarly integrated, so I will limit my discussion to FDA's role in relation to pesticides in food.

Prior to December 2, 1970, FDA established standards of analysis and set tolerances for residues of pesticides in foods, as well as performing any necessary enforcement functions. As of December 2, we have only the latter responsibility with the other functions transferred to the Environmental Protection Agency. But again, it is like the overlap between the assigned topics in this course - we can't really separate these functions. The only thing we can do is for the agencies to work closely together.

Of course, there are also other problems. Pesticides are chemicals. Food additives are chemicals. There are reportedly over 60,000 registered formulations of pesticides but there are less than 900 or so chemicals with pesticidal properties involved. There are over 4000 chemical entities used as food additives and FDA still has the responsibility for setting standards and tolerances for them, so we must stay in the toxicology business irrespective of pesticides responsibilities.

We will continue to monitor the food supply for pesticide contamination. This is done through the so-called "Market Basket Survey." This survey is described and its progress followed in a series of six papers cited in the bibliography below. In brief, it consists of samples of 82 different food items purchased in the regular retail market which are prepared as they would be for consumption. Composite samples of twelve classes of foods are slurried, saving back aliquots of the individual items for later analyses if indicated, and these slurries are tested by various standardized analytical procedures for a long list of pesticides. Analytical procedures are being improved constantly so that it is difficult to compare reliably the older figures with the recent ones, but the analyses are valuable nonetheless. Recently, we have added the heavy metals to this analysis and I'm sure Dr. Kolbye will tell you about the problems encountered there.

In late winter, 1969, DDT was found in coho salmon from Lake Michigan in quantities considerably in excess of the guideline which had been established for fish. This was the opening gun for the current battle against pesticides. I think you appreciate the term "guideline."

There is no established tolerance for DDT in fish since the DDT is not used in connection with production of fish but is accumulated in the food chain. Mr. Baker may have reminded you that, although adventitious pesticides in food are just as truly food additives as intentional ones, they are not subject to the Delaney clause in the Food, Drug and Cosmetic Act as amended, February 1969. Thus, although DDT has been designated a carcinogen (Innes, et al, National Cancer Institute 42:1101-1114, June 1969) food inadvertently containing DDT is subject only to guideline levels established by FDA and generally followed by the States.

It is as the adventitious additives that pesticides are most vexing. The idea for establishing tolerances on foods where pesticides are used directly (and presumably are necessary) is to keep the tolerances as low as possible while still allowing an adequate supply of the food involved. Although occasionally tolerances are raised, the usual pattern is one of decreasing tolerances as growers are pressured into more discreet and proper usage of pesticides. With the adventitious presence of pesticides, it is sometimes impossible to tell the source of the contaminant pesticide and, of course, equally impossible to control it. This is the principal reason for recommending a phase-out of the "hard" pesticides. As far as man is concerned, it is doubtful that a pesticide safer than DDT exists, but it has wreaked havoc on shellfish and various other susceptible organisms.

What do we do about food contaminated with pesticides that have been shown to produce adverse effects upon experimental animals, particularly when these effects resulted from administration of excessive amounts of the pesticide by bizarre routes such as DMSO injected intraperitoneally?

Naturally, we should avoid the unnecessary use or exposure to the pesticide but this may not be possible. If we are to avoid DDT, or PCB's, we may get pretty hungry or even malnourished. A concurrent action must be to try to ascertain the dosage that triggers the adverse effect. The concept that carcinogens are carcinogens at all dosage levels is being seriously questioned but still is in controversy. One school of thought holds firmly to the need to continue screening the chemicals to which we are exposed for carcinogenic, teratogenic, or mutagenic effects, using exquisitely sensitive animals and prodigious doses. Another, and rapidly growing, school feels that at least an equal share of our resources should be devoted to trying to find out the conditions under which already identified carcinogens actually produce cancers.

To accomplish the latter will require a rather radical departure from traditional toxicological testing procedures that have been used in screening for carcinogens. I would not wish to detract from the benefits that these heroic procedures have produced. By using maximally tolerated doses over long periods of time in highly susceptible animals, it has been possible to produce significant results with relatively few animals. By keeping the animal cost per test at a low level, it has been possible to test a large number of chemicals.

FDA plans to devote a substantial share of its meager resources to an attempt to realistically assess the effects of long-term exposure of experimental animals to chemicals in low concentrations similar to those encountered by man. This will require large numbers of animals handled in precisely defined protocols in order to achieve significant results. With a little luck, we hope to be under way within a few months.

With definitive information on the dose-response relationship for a variety of pesticide contaminants, together with epidemiological appraisals of human effects in areas of high exposure, it is hoped that we can identify levels of pesticide contamination that pose no danger to man. If we don't succeed in this endeavor, there will be an inevitable and accelerated food shortage as a result of our failure. It can happen either through a curtailment of effective pesticide usage or through the removal from the consumer of quantities of contaminated food. In either event, the cost will be high.

As supplemental reading and a source of bibliographic references, I recommend several government reports listed in the bibliography below.

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Pesticide Contaminants in Water and Mud and Their Environmental Impact

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INTRODUCTION

Contamination of the environment by pesticides has been a subject of mounting concern for over twenty years. Within the past year we have seen this concern, largely focused on DDT, reach a pitch where an aroused public is demanding action. This is indicated by the frequency and nature of news coverage in the Nation's press, the appointment of committees at the highest levels of Government to consider the problem, and the number of restrictive bills prepared for presentation to various State legislatures and to the Congress. Arizona, in January 1969, banned the use of DDT for agricultural and commercial purposes for a one-year trial period and Michigan has restricted its use to control of mice and bats and for emergency public health purposes on approval of application. By late 1969 it seemed evident that the Federal Government would call for phasing out most DDT for domestic usages. Similar restrictions may also be imposed on the use of DDD (TDE) and the herbicide, 2,4,5-T.

DEFINITION OF THE PROBLEM

Pesticide Production & Usage

Many of us are accustomed to thinking of pesticides in general as water pollutants. To place the issue in the proper prospective we must first consider a few basic facts.

Although the United States' production of pesticides exceeded a billion pounds in 1967, about 40 percent was exported (Mahan, Fowler and Shepard, 1968).

There are about 750 basic pesticidal chemicals (Gunther, Westlake and Jaglan, 1968), but less than half that number were registered for use and covered by legal tolerances or exemptions in the U.S. in 1966 (Westlake & Gunther, 1966).

Only 27 pesticides accounted for nearly 54 percent of the tonnage manufactured in the U.S. in 1967 (Mahan, Fowler and Shepard, 1968). These included 14 insecticides, eight fungicides, and five herbicides.

From these data it may be concluded, at least with respect to the quantities of pesticides used within the United States, that the potential of widespread water pollution is currently limited to a relatively few compounds. These data, however, do not preclude the possibility of local pollution problems associated with the manufacture or processing of any pesticide, or from accidental spills, or careless use.

Environmental Contamination and Significance

The acute effects of gross pesticide pollution are well known and depend upon the toxicity of the compound in question and its concentration in the environment. Widespread and chronic environmental pollution problems usually involve only those pesticides and degradation products that are: (1) toxic, (2) persistent, (3) in widespread and voluminous use, and (4) have the ability to be taken up and concentrated in living organisms. This latter phenomenon has been called "biological magnification." The pesticides most frequently involved are the organochlorine insecticides: DDT, DDD (TDE), endrin, heptachlor, aldrin, dieldrin, chlordane, toxaphene, Strobane, and BHC or its gamma isomer, lindane (Nicholson, 1969). More recently, the organic mercury compounds have been implicated (Smart, 1968; Novick, 1969).

Among these compounds, DDT has been the most objectionable. The universal occurrence of traces of DDT is now common knowledge. It is used throughout much of the world and its secondary dispersion is aided by wind, water, soil, plants, and the movement of animals in which residues have accumulated.

We are faced with mounting evidence that traces of DDT are not as innocuous as many have believed. DDT transmitted through the ovaries was shown to be responsible for significant losses of lake trout fry in a New York fish hatchery (Burdick, et al. 1964), and investigations are being made to determine if losses of coho salmon fry in Michigan hatcheries are similarly caused.

A drastic decline in populations of fish-eating raptorial birds, such as the bald eagle and osprey, has long been associated circumstantially with the advent and use of DDT. Only recently has supporting evidence been produced to suggest that DDT and its metabolite, DDE, can cause an imbalance in calcium metabolism resulting in egg shell thinness and loss of eggs in the nest through breakage (Hickey and Anderson, 1968). The hypothesis that sublethal amounts of persistent chlorinated hydrocarbon pesticides are involved is further strengthened by experimental studies with dieldrin and DDT using captive sparrow hawks (Porter and Wiemeyer, 1969).

As a final example, 28,000 pounds of coho salmon caught commercially from Michigan streams was seized by the Food and Drug Administration in March 1969 because the fish contained up to 19 parts per million (ppm) of DDT, an amount deemed to be excessively high (Congressional Record 1969). This seizure was a severe blow to commercial fishing and also to recreational interests of the states adjacent to Lake Michigan as this new fishery was proving to be an economic bonanza (Henkin, 1969).

You will note that in each of these instances of insecticide related loss, the insecticide must first have entered the water.

Concentrations in Water

A synoptic survey for chlorinated hydrocarbon insecticides in waters of 56 of the Nation's major drainage basins and three of the Great Lakes was made by the U. S. Public Health Service on whole water samples collected during the period of September 18-29, 1964 (Weaver, et. al; 1965). The samples from 96 sites in 41 States were analyzed by thin layer chromatography and microcoulometric titration gas chromatography. The wide distribution of dieldrin, endrin and DDT with its metabolite, DDE, is significant (Table 1). Concentration values in water in all samples were less than one part per billion (ppb).

Similarly, the U. S. Geological Survey in October 1965 began the collection and analysis of water samples with associated suspended sediment from selected streams west of the Mississippi River (Brown and Nishioka, 1967; Manigold and Schulze, 1969). The samples, taken monthly, were examined by electron capture gas chromatography for the common chlorinated hydrocarbon insecticides and for the herbicides 2,4-D, silvex and 2,4,5-T. Results of the first year's work on ten rivers are summarized in Table 2, and those for the subsequent two years from 19 rivers are given in Table 3.

All twelve pesticides or derivatives were recovered at one time or another. Sixty-six percent of 114 water samples taken during the first year were positive for one or more pesticides. Forty-nine percent of 33 samples were positive in the subsequent two-year period. Concentration values all were less than one part per billion.

Lindane, dieldrin and heptachlor epoxide were recovered most frequently during

TABLE 1

CHLORINATED HYDROCARBON INSECTICIDES AND RELATED COMPOUNDS IN MAJOR RIVERS OF THE UNITED STATES[1]

Compound	Geographic Distribution (No. States with Positive or presumptively Positive samples)	No. Rivers and Lakes Positive	Sampling Stations Positive	
			No.	Positive and Quantified Range ppb[2]
dieldrin	36	39	56	0.002–0.118
endrin	28	23	30	0.003–0.094
DDT	28	22	23	0.007–0.087
DDE	28	17	18	0.002–0.018
TDE	1	1	1	0.083
aldrin	10	1	1	0.085
heptachlor	16	0	0	–
heptachlor epoxide	0	0	0	–
BHC	2	0	0	trace

[1] Except Alaska and Hawaii. Adapted from data in "Chlorinated Hydrocarbon Pesticides in Major U.S. River Basins" by Weaver, Gunnerson, Breidenbach, & Lichtenberg. Public Health Rpts. 80:481–493. 1965.

[2] Minimum detectable concentrations of dieldrin, endrin, DDT, DDE, aldrin and heptachlor ranged from 0.002 to 0.010 ppb. Comparable values for TDE, heptachlor epoxide and BHC were 0.075, 0.075, and 0.025 ppb, respectively.

TABLE 2

PESTICIDES IN TEN SELECTED WESTERN STREAMS, 1965 - 1966[1]

Compound	No. Samples Positive of 114 from Eleven Stations	Range of Concentration in Parts Per Billion
lindane	46	0.005–0.020
dieldrin	29	0.005–0.015
heptachlor epoxide	20	0.005–0.090
DDE	18	0.005–0.020
DDT	14	0.025–0.110
heptachlor	14	0.005–
TDE	14	0.005–0.015
endrin	7	0.010–0.015
aldrin	4	0.010–0.040
2,4-D	0	–
2, 4, 5-T	0	–
silvex	0	–
	75 positive for one or more pesticides	0.005–0.110

[1] Adapted from data in "Pesticides in Selected Western Streams. A contribution to the National Program" by Brown and Nishoika. Pesticide Monitoring Journal 1 38–46, 1967.

the period October 1965 through September 1966. During the following two years DDT, DDE and the herbicide 2,4-D were most commonly found. No explanation was offered for this difference in frequency of recovery.

The concentration of chlorinated hydrocarbon insecticides in water alone, however, does not necessarily correctly reflect the availability of these compounds to living

TABLE 3

PESTICIDES IN NINETEEN SELECTED WESTERN STREAMS, 1966–1968[1]

Compound	No. Samples Positive of 333 from 20 Stations	Range of Concentration in in Parts Per Billion
DDT	82	0.01–0.12
DDE	49	0.01–0.06
2, 4-D	41	0.01–0.35
TDE	35	0.01–0.04
2, 4, 5-T	28	0.01–0.07
heptachlor	27	0.01–0.04
dieldrin	24	0.01–0.07
silvex	14	0.01–0.21
lindane	13	0.01–0.02
aldrin	11	0.01–0.04
endrin	4	0.01–0.07
heptachlor epoxide	2	0.01–0.04
	75 positive for one or more pesticides	0.01–0.35

[1] Adapted from data in "Pesticides in Selected Western Streams–A Progress Report" by Manigold and Schulze. Pesticide Monitoring Journal 3:124–135. 1969.

components of the hydrosphere. Studies in the major agricultural river basins of California have indicated that an average pesticide concentration of 0.10 ppb to 0.20 ppb in water may mean that bottom sediments contain 20 ppb to 500 ppb of the compounds (Bailey, T. E. and Hannum, J. R. 1967).

A pond near Denver was treated with 0.02 ppm of DDT, and the insecticide was quantified in water, mud, vegetation, fish, and crayfish for 16 months (Bridges et al. 1963). As the DDT residues in the water decreased to none detectable at four weeks, residues in the mud increased to 8.30 ppm at 24 hours and disappeared in 12 months; vegetation residues were 30.7 ppm within 30 minutes and decline to 0.6 ppm at 12 months; rainbow trout, black bullhead, and crayfish still contained DDT and the metabolites TDE and DDE at 16 months.

DDT is remarkably hydrophobic and does not remain in water in very large quantities. It tends to concentrate and persist in other compartments of the hydrosphere. Such data gives reason to pause and reconsider whenever the urge strikes to set permissible limits for this and similar compounds in water alone where the objective is to maintain a suitable overall environment for aquatic life.

SOURCES OF WATER CONTAMINATION

Pesticides may enter water in a variety of ways. They are carried in runoff from the land, discharged in industrial waste; dumped through carelessness and accidents, and direct application to water to control unwanted plant and animal pests (Nicholson, 1969). Other sources may be airborne residues, home use and garbage disposals (sewers), dumping of products containing residues higher than tolerances. dead animals and animal excreta, and decaying plant tissues (Westlake and Gunther, 1966). The significance of these additional sources remains to be more fully documented, but their validity as sources is not questioned. Contamination may be more or less continuous, generally at very low levels (less than one part per billion), or in brief instances contamination may reach concentrations sufficient to kill fish and other aquatic life.

Runoff

Let us first consider runoff from the land. This is probably the single most widespread and significant source of low level surface water contamination by pesticides (Nicholson, et al, 1962; Nicholson, et al, 1964; Hindin, May and Dustan, 1964; Lauer, et al, 1966; Nicholson, Grzenda, and Teasley, 1966; Bailey and Hannum, 1967). Runoff may be more or less continuous throughout the year at levels generally less than 1 ppb or it may occur sporadically (Nicholson, 1969). Transport from land to water may occur while the pesticide is adsorbed on eroded particulate matter, while in solution in runoff water, or by both means. Recently it has been shown that sodium humate, a common soil constituent, solubilizes DDT in water (Wershaw, Burcar and Goldberg, 1969). This phenomenon would be expected to facilitate the transport of DDT.

Factors that control the runoff of pesticides are: (1) the nature of the pesticide, (2) the extent to which it is used, (3) edaphic considerations, (4) climatic factors, (5) topography, and (6) land usage and management practices. Pesticides having short half-lives do not possess the runoff potential of persistent types. High humus type soils will yield less insecticide than will sandy soils (Lichtenstein, 1958). Heavy rainfall immediately following application of chlorinated hydrocarbon-type insecticides is a classic cause of run-off that sometimes causes fish kills (Young and Nicholson, 1951).

Industrial Waste

Perhaps the second most significant source of pesticides in water is industry. The types of industries that may be involved include producers of basic pesticides, pesticide formulators, cooperage firms that reclaim used pesticide drums, operations that apply wool preservatives, textile plants that moth-proof woolen yarns and fabrics with dieldrin, and paper manufacturing industries that use phenylmercury acetate (PMA) as a fungicide.

Releases from industrial sources may be continuous in manufacturing or process effluents, or they may occasionally be high concentration slug discharges following in-plant mishaps or breakdowns. In the latter case, biological catastrophies may result from acute toxicity in receiving streams.

As an example of a plant breakdown, an instance that occured in Alabama may be cited (Alabama Water Improvement Commission, 1961). A plant which manufactures parathion and methyl parathion normally treats its waste very effectively by neutralization with strong alkali followed by double activated sludge treatment through its own plant and that of a nearby city. During a breakdown of the industrial treatment plant in 1961 the city treatment plant could not handle the load of toxic materials and 60 percent of the combined industrial effluent containing parathion and city sewage was discharged untreated to a creek until corrective action could be taken. Fish, turtles, and snakes died along 28 miles of the stream whose average discharge at the time was 211 million gallons a day at a velocity of 3/4 mile per hour. The creek entered the Coosa River which then had an average discharge about 28 times greater than that of the creek. Even with that dilution, traces of parathion residues were recovered 90 miles down the Coosa and some lesser fish kills occurred in it. Unfortunately, water samples were not taken for analysis until the third day after fish were first observed dying. At that time a maximum of 0.21 ppm of parathion was found at a point on the creek 22 miles from the city. On that same day, 667 ppm of parathion was reported in thickened sludge at the city sewage treatment plant.

An example of pesticide accumulation from continuous discharge involved a manufacturer of DDT who provided minimal waste treatment. The DDT content of water in a ditch receiving these wastes was 0.1 ppm to 7.8 ppm. Bottom samples analyzed from 0.6 percent to 2 percent DDT along the half-mile length of this ditch after it had been carrying away wastes from this industrial plant for 1 1/2 years.*

Barthel et al. (1969), in his study of pesticide residues in the sediments of the Lower Mississippi River and its tributaries, found five pesticide formulating companies that dumped waste materials into city sewers, into channels and sloughs near their plants, and onto city and privately owned dumps where they could be washed away by rainfall. Residues found included dieldrin, aldrin, endrin, isodrin, chlordane, lindane, and DDT analogs and metabolites. Many of the residues in river bottom muds were in concentrations less than 0.05 ppm, but some ranged in the thousands of parts per million in the vicinity of the industrial plants. Most of the bottom muds were anaerobic, and the degradation products found were the same as those reported by Hill and McCarty (1967) from a study of anaerobic degradation of pesticides in sewage sludge.

Accidents and Carelessness

Although strenuous efforts have been made within agricultural and related industries to minimize accidents and carelessness with pesticides, some instances of water pollution from these causes still are reported. An instance of carelessness having potentially serious human health implications occurred in Florida in 1964 (Florida State Board of Health, 1964).

A rancher instructed his hired hand to dispose of approximately 50, four-pound bags of over-age 15 percent parathion dust. This was done without the rancher's knowledge, by dumping them from a highway bridge into the Peace River one mile upstream from the municipal water intake of Arcadia, a town of about 6,000 people. The incident was discovered when boys fishing near the bridge hooked one of the discarded bags and reported it.

The town fortunately had an auxiliary well and immediately reverted to it. The citizens were instructed not to use the water, and flushing of the water mains was begun immediately. Subsequent analysis of water samples showed that the parathion concentration in the distribution system was generally less than 1 ppb. However, a series of samples taken from a tap at the local bus station ranged from 10 ppb to 380 ppb.

Investigation revealed that the bags of parathion had been dumped in the river about 10 days before their discovery. They were polyenthylene lined and resisted rapid disintegration. All but 8-12 bags were eventually recovered. Those unrecovered bags that disintegrated apparently did so over a period of several weeks. This may have been the reason that residue levels were never sufficiently high to be a threat to human health or to fish in the river. Parathion residues occured in the river for about two weeks after the discovery at concentrations generally less than 1 ppb.

Accidents also have caused real or potential water pollution problems. In March of 1965, during the night, 2500 to 3000 pounds of five percent chlordane wettable powder spilled from a truck passing through Orlando, Florida. After recovering what could be salvaged, about 1300-1700 pounds was hosed into the street's storm drainage system from which it passed into a dry creek bed not far from one of the city's lakes. When the potential for damage to the lake was realized, the contaminated water and soil were removed for safe disposal elsewhere.

Other Sources

The chemical control of aquatic weeds, rough fish, and aquatic insect pests often results in some pesticide residue in water. These activities are generally managed by professionals so that undesirable consequences are minimized. Toxaphene, however, which was first used for control of rough fish in lakes in the early 1950's, has sometimes caused trouble. Although toxaphene treated lakes may generally be re-stocked within six months to a year after treatment, occasionally a lake may remain toxic to re-stocked fish for five years (Kallman, Cope and Navarre; 1962; Terriere et al., 1966). Such was the case at Miller Lake in Oregon that was treated in 1958 at an estimated rate of 40 ppb. The initial residues declined sharply to less than 2 ppb and remained near that level for approximately five years (Terriere et al., 1966).

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*Personal communication from Charles Kaplan, FWPCA, Southeast Region, Atlanta, Georgia.

Local drift of dusts and sprays from areas of pesticide application is well known and can also be a source of water contamination.

Urban storm water has also been suggested as a carrier of pesticides (Wiebel et al., 1966). The significance of urban sites and activities as sources of water pollution by pesticides is now being investigated at Michigan State University.

CONTROL OF PESTICIDE POLLUTION

Can anything practical be done to control water pollution by pesticides? The answer is most definitely yes!

Point sources can be controlled most easily. These are industrial sources where waste effluents enter watercourses through single or multiple outfalls. A variety of effective waste treatment systems are now employed. Research and demonstration grant funds are available through the Federal Water Pollution Control Administration for studies leading to the development of new or improved waste treatment measures. Research on the chemical degradation of pesticides is expected to result in knowledge that can be engineered into new and effective treatment technology.

Since the more persistent chlorinated hydrocarbon insecticides are recognized as being more troublesome than less refractory pesticides, their usage can be minimized or reserved for those purposes where adequate substitutes can not be found.

Advanced concepts of pest control are being developed that range from male sterilization techniques to use of micro quantities of pesticides that are just as effective yet not as wasteful of toxicants as are present methods of application. The acceptance of pest control at somewhat less than eradication levels is also being emphasized. This concept involves reduction of pest population levels only to that point where economic loss will not result.

Scientists at the Southeast Water Laboratory are at work to develop a means to preduct runoff pollution and to prevent it from occurring (Nicholson, 1969). The Universal Soil Loss Equation, developed by soil conservationists to guide conservation farm planning throughout the United States (Wischmeier and Smith, 1965), is being considered as the basis for a new formula for predicting pesticide loss from the soil. Knowing what to anticipate, control would be accomplished by using recommended chemicals and practices.

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CHANGING PESTICIDE PATTERNS

Dr. L. C. Gibbs

My assigned topic is somewhat like an octopus. There are so many facets to it that you don't know where to grab hold and get started. Irrespective of my dilemma, I'll start off by saying that we've been experiencing changing pesticide patterns for years so changes as such don't really bother me. On the other hand, if we had looked at the rate of change, volume and kinds used, application techniques, effect on non-target organisms, persistency and other aspects, we would have been more concerned and some of the actions taken recently might have developed earlier.

Everyone pretty generally agrees that pest control is essential for protecting man, plants and animals from diseases, discomforts or annoyances and for insuring the production of an adequate supply of high quality food and fiber. The continuing need for pesticides has also been indicated in a number of studies. Included are the Ribicoff Committee (1964), two committees of the National Academy of Science-Pesticides in Foods and Feeds (1968) and Persistent Pesticides (1969), and the Mrak Commission (1969). These reports pointed out existing, as well as potential, problems which we are having to cope with today. Increasingly, emphasis in research, regulation, education and operating programs is being directed toward practicing and encouraging the use of the most effective means of pest control and/or management which will cause the least potential hazard to man, his animals, fish, wildlife and other components of the environment. In keeping with this policy, persistent pesticide uses have been and will continue to be reviewed use by use and only those uses considered essential and for which no substitutes are available will be retained. This means that many of the chemical uses producers have become accustomed to will be lost--some because there are safer less persistent substitutes and others because of their deleterious and cumulative effects on certain species of fish, wildlife, etc. and possible effects on man.

Today, pest control in the U.S. is practiced in the setting of a population growing in numbers, density, and affluence and with an intensified monocultural system of agriculture which is employing fewer and fewer people. Under this situation, we have perhaps placed too great a reliance on pesticides following the initial success of the new organic pesticides and the development of more efficient application techniques. The change in the pesticide patterns which have taken place over the years didn't just happen. They have been predicated and based on developments in research, technological advances, legislation, labor shortages, labor costs, economics, our system of agriculture, food standards, and other aspects related to an affluent society. To these, we must add another far-reaching consideration--concern for the environment. All points considered, we might say that our changing pesticide patterns, like other developments, are merely a reflection of the time and period in which we live.

In order to grasp the full significance of some of the developments that have taken place which have been instrumental in effecting changes in our pesticide use patterns, we need only to recall some of the major changes that have taken place in agriculture. Perhaps the first one we should note is that in the early history of agriculture, farming was diversified and our pest control knowledge and chemicals were limited to say the least. Even in the early 40's, we could still count our pest control materials on our fingers and the commonly available materials included items such as lime sulfur, Paris green, lead arsenate, nicotine sulfate, Rotenone and a few others. In contrast today, our pest control arsenal consists of over 250 basic chemicals available in some 45,000 registered products. Needless to say, almost everything has changed. Foremost among the factors which have been influencing changes in pesticide use patterns has been the shift toward development of an intensive monoculturistic system of agriculture. This system, for the sake of economy, has resulted in the concentration and culture of large blocks or acreages of a single or successions of the same crop. This alone has been conducive to a build-up of certain pests which required more pesticide use and in some cases resulted in the development of resistance to certain pesticides within some insect species. Increased production costs resulting from labor shortages, increased labor costs, etc. have also been conducive to mechanization and this in turn has fostered increased plant populations which further contributes to increased insect and disease problems. So you see, the circle goes round and round and never stops or stands still. Other factors include the passage of more stringent regulations and laws governing the registration, transportation, sale and use of pesticides, lowered residue tolerances, and the development of the carbamate and systemic type pesticides. One other factor which I have so far failed to mention specifically is the advances made in our analytical equipment and technology. Each factor or combination of factors in turn affects use patterns one way or another and the full impact or change can seldom be fully determined because of the complexity and interaction involved.

Any discussion of changing pesticide patterns would be remiss without some mention of use statistics and recent legislative and regulatory developments. First let's look at some aspects of use statistics since this is undoubtedly the area which has contributed most to some of our problems. Use, likewise, has without question been the paramount factor responsible for the tightened legislative and regulatory actions which have been affected in the last few years. In looking at use statistics, I think that it is important that we look at the volume used and note the use trends developed within the three major classes of pesticides and within even a single class. The following tables, which are more or less self-explanatory, show what the use patterns and trends have been over the years for pesticides as a whole and for some within a group or class. See Table 1 for statistics on pesticide sales volume for fungicides, herbicides and insecticides. Table 2 is illustrative of trends and use patterns developed for the organochlorine type insecticides.

Table 1. Sales of organic pesticides by primary chemical manufacturers according to type of usage, 1962-1968

Type of Usage	1962		1963		1964		1965	
	Amount	% of Total	Amount	% of Total	Amount	% of Total	Amount	% of Total
	(Volume of sales in 1,000 pounds)							
Fungicides	97,589	15.4	93,265	14.3	95,556	13.8	106,342	13.9
Herbicides	95,209	15.0	122,872	18.9	152,027	21.9	182,869	23.9
Insecticides	441,164	69.6	435,334	66.8	444,772	64.3	474,694	62.2
TOTAL	633,962		651,471		692,355		763,905	

Type of Usage	1966		1967		1968*		1969	
	Amount	% of Total	Amount	% of Total	Amount	% of Total	Amount	% of Total
	(Volume of sales in 1,000 pounds)							
Fungicides	118,397	14.4	120,413	13.4	128,961	13.5		
Herbicides	221,502	26.9	287,582	32.1	318,554	33.2		
Insecticides	482,357	58.7	489,368	54.5	511,116	53.3		
TOTAL	822,256		897,363		958,631			

*Preliminary Data

The use of persistent pesticides underwent more intensive discussion in 1969 than ever before. Although pesticides have contributed tremendously to preventing human disease and to increasing the production of food and fiber, mounting evidence indicated the need for concern about unintended effects on the environment, including injury to the health of man and livestock. Associated with the benefits from the use of pesticides are the risks of injury; and these risks are greater from the use of persistent chemicals. Restrictions have now been placed on the latter with special emphasis on DDT. Coupled with this have been numerous State legislative actions which relate to pesticide use, sale, record-keeping, applicator licensing, development of restricted use categories, etc. In this respect it is of interest to note that as of November 1970, 36 states had enacted pesticide applicator licensing laws. Other significant developments include complete restriction on the use of DDT in a number of states and the development of lists of chemicals limited to restrictive or permit uses.

U.S. production of pesticides continued to increase in 1968 to meet the rising consumer demand both at home and abroad. Production of synthetic organic pesticides increased 14 percent. The average annual growth was nearly 8 percent during the previous five-year period. Production of insecticides in 1968 increased 15 percent; herbicides, 17; and fungicides, 7.5. Available production data are limited mostly to synthetic organic pesticides. Statistics for them provide a good indication of growth, however, since they constitute an estimated 90 percent of U.S. pesticide production.

Evidence continues to accumulate showing that persistent ("residual," "long-lasting," "long-lived," or "hard") pesticides are contaminating the environment and adversely affecting various life forms within it. Persistent pesticides are those which dissipate or degrade slowly and whose residues remain in decreasing but measurable concentrations for varying periods of time, usually into the second growing season or longer. They are disseminated by natural forces and have characteristics that favor their accumulation and storage in living organisms.

The major persistent pesticides are commonly known as "organochlorine" compounds ("chlorinated hydrocarbons" or "polychlors"). They include aldrin, benzene hexachloride, chlordane, DDD, DDT, dieldrin, endrin, heptachlor, lindane, toxaphene, and certain others. Compounds containing arsenic, copper, lead, and mercury are also persistent.

In recent years, DDT has become a prime target of concern. Its usage began earlier and has been more widespread than that of other major persistent pesticides. For well over two decades, DDT has been the most generally effective and most widely used pesticide worldwide. It is best known for practically wiping out malaria in the United States and over large areas elsewhere. It has been a valuable tool in combating cholera, typhus, Rocky Mountain spotted fever, and encephalitis. Uninhabitable areas have been made more habitable and life has been made more comfortable for many people. DDT also has worked wonders for farmers. Its use has controlled many major insect pests, notably those troublesome to cotton, vegetables, and fruit.

Few food-producing areas are free of DDT contamination. There has been awareness of this for some years. The President's Science Advisory Committee in 1963 called attention to low-level contamination of the environment with DDT. As long as two decades ago, DDT residues in milk caused restriction to be placed on its use for controlling flies and other insects on dairy cattle.

Use of certain other organochlorines on forage grazed by dairy cattle was restricted for the same reason; namely, that residues appeared in milk.

Use of DDT in the United States during crop year 1968 was only 42 percent as much as in 1959. Its use peaked in 1959 at more than 78 million pounds but declined to less than 33 million by 1968.

Other organochlorine insecticides were developed following the introduction of DDT. The total usage of the more widely applied of these insecticides, including DDT, also peaked in 1959 at 156 million pounds but was down to 71 million in 1968 (Table 1). The 1968 level is only 46 percent of the 1959 usage, close to the 42 percent for DDT. Largely responsible for this decline are (1) increased insect resistance to insecticides, (2) the availability of less persistent insecticides which are efficient in insect control, and (3) the concern about the risks from use of persistent insecticides.

Much of the contamination from persistent pesticides may have resulted from excessive use. Although environmental contamination from past usage will continue for a period of years in lessening amounts, further reductions in usage and careful application of all pesticides can be expected to substantially lessen this type of pollution of the environment.

Table 2. Organochlorine insecticides: Producers' domestic disappearance of selected kinds by crop year, United States, 1955-1968

Crop year 1/	Aldrin-toxaphene 2/ group	DDT	BHC	Total
	1,000 pounds	1,000 pounds	1,000 pounds	1,000 pounds
1955	54,400	61,800	7,800	124,000
1956	61,570	75,000	9,450	146,020
1957	52,500	71,000	6,600	130,100
1958	78,834	66,700	5,500	151,034
1959	73,331	78,682	4,276	156,289
1960	75,766	70,146	5,111	151,023
1961	78,260	64,068	4,577	146,905
1962	82,125	67,245	2,404	151,774
1963	79,275	61,165	1,299	141,739
1964	83,161	50,542	3/	133,703 4/
1965	80,568	52,986	3/	133,554 4/
1966	86,646	46,672	3/	133,318 4/
1967	86,289	40,257	3/	126,546 4/
1968	38,710	32,753	3/	71,463 4/

1/ Ends September 30.

2/ Includes aldrin, chlordane, dieldrin, endrin, heptachlor, Strobane and toxaphene.

3/ Not published separately to avoid disclosure, but probably less than in 1963.

4/ Includes only the aldrin-toxaphene group and DDT.

Progress with Less Hazardous Controls. Research has already developed chemicals suitable for use to control many target pests and which are less persistent and more specific than the organochlorine insecticides. Readily degradable chemicals and biological, physical, and cultural controls as an integrated assault offer areas for research into possible answers to many uses of persistent pesticides. The emphasis on newer weapons includes the study and development of viruses causing insect diseases, sterilization of adult insects to disrupt their reproductive cycle, synthesis of natural insect attractive scents or effective substitutes as lures, ultraviolet light and ultrasonic sound as control agents, hormones that interfere with normal insect growth, and the manipulation of genes. Further research is being stimulated in the breeding and utilization of domestic and imported predatory and parasitic insects, long used as essential biological aids in the control of a number of insect pests.

Outstanding achievements include massive releases of sterilized male screwworm flies which have virtually wiped out this enemy of the southern and western cattle industry, and the application of milky disease spores which have infected and killed Japanese beetle grubs in the soil.

Selected examples of activities designed to control pests without using toxic chemicals or with reduced or limited amounts follow:

BIOLOGY AND CHEMISTRY

Control of Insect Diapause (resting state) by Light. Recent tests have determined the most effective wavelengths of light for breaking diapause of codling moth larvae and oak silkworm pupae. Diapause was prevented in some European corn borer larvae and imported cabbage worm pupae in an outdoor pilot test by extending day length. Similarly, diapause in pink bollworms was prevented in laboratory tests by short light periods at certain times during the dark cycle.

Effects of Light. Adverse effects of continuous light on the reproductive systems and mating behavior of the Indian-meal moth have been demonstrated. Light intensities of 200-foot candles or more inhibit or reduce egg laying by 25-50 percent of that occurring in the dark. Females inhibited by light normally retain their eggs until the day before their death and these eggs, laid under stress, show a very low percentage of hatch. Adults emerging from cultures reared in continuous light were slow to mate. Experimentation and morphological examination have shown that oviposition is triggered by the quantity of the spermatozoa in the spermathecae and not by the physical stimulus of the copulation. Further studies have shown that males reared under continuous light transfer very few spermatozoa to the females. The integration of these effects of the light regime offers considerable promise as a new method or as an adjunct to existing methods for controlling the Indian-meal moth.

Insect Hormones as Potential Control Agents. The natural ecdysones (molting hormones) and/or certain of their synthetic analogs cause termination of pupal diapause in a number of insect species. Studies on the mode of action and metabolism of radioactively labeled synthetic ecdysone analogs revealed that such compounds or their metabolites trigger the biosynthetic mechanism for the synthesis of the insect's own hormones. If metabolites of natural or synthetic ecdysone analogs that inhibit larval growth and reproduction can be found whose biological activity is greater than the parent compound, such chemicals might well serve as models for the preparation of safe and more potent agents for insect control.

Promising Biological Control Agents for Control of Aquatic Weeds. Studies of the *Marisa* snail in laboratory, greenhouse, and outdoor pools have shown considerable promise for its use in controlling submersed aquatic weeds in warm waters. More limited studies show the *Pomacea* snail to be even more effective in feeding on important aquatic weed species.

The white Amur fish which is indigenous to certain rivers in Siberia and northern China has given outstanding promise for control of aquatic weeds in experiments in European and some Asian countries. This fish is being used quite extensively in both temperate and subtropical areas of Asia for control of aquatic weeds and is an important food fish.

New Herbicide Formulation and a Combination Promise Greatly Increased Effectiveness and Safety in Control of Aquatic Weeds. A combination of 4 ppm of $CuSO_4$ and 1 ppm of diquat gives more positive and lasting control of hydrilla than 20 ppm of $CuSO_4$ or 3 ppm of diquat alone or than any of the many other herbicides and combinations that have been tested. The combination provides greater safety for fish, reduces the chemical cost considerably, and greatly reduces the chemical residues in water.

A new granular formulation of an amine salt of endothall provides control of hydrilla comparable to the much higher rates of liquid formulations previously used, confines the chemical residues mostly to the bottom two feet of a lake or pond, reduces the amount of herbicide required, and eliminates or greatly reduces the fish toxicity involved in use of liquid formulations.

Biochemical Factor in Corn Provides Resistance to European Corn Borer. A natural constituent of corn DIMBOA has been found responsible for resistance to the European corn borer and may help scientists breed superior resistance into hybrid lines. During the recent research, an accurate, objective method was developed for determining the DIMBOA in corn. This enables new lines of corn to be screened chemically for corn borer resistance. This is more rapid than the previous visual screening and its correlation with the visual screening of field plants was very high.

Uptake of a Systemic Fungicide by Elm Seedlings. Benomyl may be a promising fungicide for the control of Dutch elm disease. Benomyl was readily taken up by the seedling roots and by a newly developed technique, detected throughout the plant. The recent discovery and development of several systemic fungicides have given new impetus to the search for chemotherapeutic agents which will control the Dutch elm disease. This approach is especially significant since DDT up until recently has been the major chemical control for this pest.

Microbial Insecticide Lethal to Defoliators. Continuing studies of the pathogenicity and mode of action of Bacillus thuringiensis in forest insects have shown that the spores and crystals produced by the bacterium affect insects in different ways. The western hemlock looper is killed by the crystals alone; Douglas-fir tussock moth, western tent caterpillar, and the gypsy moth are most susceptible to the spores and crystals combined. Chemical constituents of host tree foliage affect pathogenicity, also.

A Highly Virulent Strain of Bacillus Thuringiensis, Designated as HD-1. Two commercial companies produced pilot plant quantities of HD-1 which were supplied to qualified research workers at several locations. Test results are extremely promising for control of cabbage looper and Heliothis spp. Progress is being made toward standardizing formulations in terms of International Units per milligram of the delta endotoxin.

Biological Control of Imported Cabbageworm. Imported cabbageworm (Pieris rapae) was effectively controlled by innoculative releases of the egg parasite, Trichogramma evanescens and the larval parasite, Apanteles rubecula, by maintaining the host population at a sufficiently high level to provide an adequate constant food resource for the parasite. This was accomplished by programmed releases of reared adult Pieris rapae.

Control of Lepidopterous Insect Populations with Inherited Sterility. Although moths are more resistant to radiation sterilization than other insects, they were found to be prone to pass on to their progeny radiation damage causing sterility in the next generation. In contrast to fully sterilized moths, which were noncompetitive, cabbage looper moths treated with three-sevenths of a sterilizing dose were able to compete with normal moths for mates. In laboratory and preliminary field cage tests, both male and female progeny of irradiated males were almost completely sterile, preventing a population increase in the second generation. Additional research is needed to determine if this technique can be used for practical control of insect pests, as a contribution to the development of new methods of control that will not adversely affect other organisms or pollute the environment.

Insect Attractants. New synthetic attractants much superior to those currently in use were discovered for European chafer, Japanese beetle, and yellow jackets. Four terpenoid compounds were isolated from male boll weevils which when properly combined attract both male and female weevils; the compounds were identified and synthesized. The synthetic material was highly promising in limited field tests. Commercial production of the attractant will provide material for use in an extensive field study to determine the feasibility of eradicating the boll weevil in an integrated program utilizing several methods to destroy the weevil.

Importation of Insect Parasites. Over 125,000 living specimens of 33 exotic or recently established parasites and predators were distributed for release in 29 states to aid in the control of 15 kinds of insect pests. Reports from cooperators during the year indicate new establishments of parasites that attack cereal leaf beetle, alfalfa weevil, elm bark beetle and greenbug in Michigan, Virginia, Ohio, and Oklahoma respectively.

Biological Control of Nematodes. Heavy application of chitin to field soil controlled root-knot nematodes on tomato; this was due to microbial activity of chitinoclastic actinomycetes. Control of root-knot lasted for two years. Several ammonium fertilizer salts controlled root-knot in pot test, but were inconsistent in field tests. Radio-labeled EDB and DBCP was taken up by nematodes and nematode-trapping fungi; there was no appreciable lethal effect on the fungi, indicating these nematicides will not destroy these beneficial soil fungi. Culture filtrates from Aspergillus niger were toxic to citrus and lesion nematodes. Chromatographic analysis of filtrate and subsequent tests indicate that oxalic acid was the toxic fraction contained in the filtrate.

Release of New Inbred Lines and Hybrids Resistant to Pests. Thirteen new inbred lines or varieties of cereal grains with specific resistance to certain diseases and insects were released in FY 1969 by the U.S. Department of Agriculture in cooperative Federal-State programs.

Biological Control of Alfalfa Weevil. Indications are that 5 European parasites of the alfalfa weevil introduced during the past 10 years are definitely responsible for reduced weevil populations in alfalfa fields in the Mid-Atlantic States, where most of the releases have been made. Virtually no insecticide applications were required to control the weevil in Delaware during 1969; treatments were required in only 20-30% of the fields in New Jersey and Pennsylvania. In contrast, 5 years ago, nearly all alfalfa fields in these three states required insecticide treatments to prevent crop loss.

Insect and Disease-resistant Alfalfa Germplasm Pools Released. Two pools of alfalfa germplasm, MSE-6 and MSF-6, were released cooperatively with the Nevada Agricultural Experiment Station to plant breeders. MSE-6 and MSF-6 are vigorous populations with broad genetic bases that possess resistance to the pea aphid and to biotypes ENT-A and ENT-B of the spotted alfalfa aphid. They are moderately resistant to bacterial wilt and stem nematodes. The damage that the spotted alfalfa aphid causes to alfalfa is estimated at $26 million annually. Resistant varieties save the grower $10 to $15 per acre in spray costs alone.

First Weevil Resistant Alfalfa Variety Released. Team, a newly released alfalfa variety with disease and insect resistance, promises better crops for growers in Maryland, Virginia, and North Carolina. The new variety is the first in certified seed production that has improved resistance to the alfalfa weevil, which causes yield and quality losses of some $57 million annually, exclusive of insect control costs. Team is highly resistant to the pea aphid and moderately resistant to anthracnose, Stemphylium leaf spot, and common leaf spot. In the mid-Atlantic area, use of Team alfalfa will reduce the need for insecticides. In Maryland, insecticide applications on this variety were not needed for control of the weevil during the past 2 years.

Sterilization of Male Boll Weevils Achieved. Busulfan, fed to adult boll weevils for 6 days as 0.1% of the diet, induced permanent and nearly complete sterility in nearly all males and caused only moderate mortality. In at least four consecutive matings, the treated males displaced normal sperm in previously mated females. The production of sex pheromone in treated males was normal.

Use of Nondiapausing Boll Weevils for Population Suppression. To survive the winter in most areas of the United States after frost has killed the cotton plants, boll weevils must be in a state of dormancy called diapause. A strain was developed in which most individuals lack the ability to diapause. In experimental field releases in Mississippi, only a small percentage of the hybrid progeny of the nondiapause and native weevils were able to survive the winter. Plans are to further evaluate the potential utility of the nondiapause strain in connection with sterile male releases.

Biological Control of Larch Casebearer is Promising. Assessment of an introduced parasite released as a bio-control agent for the larch casebearer in northern Rockies shows that the parasite has become established in 50 percent of the release plots since 1964. This combined with as much as 40 percent parasitism by native parasites looks very promising in keeping losses within tolerable limits without chemical application.

Introduced Parasite of Elm Bark Beetle Established. The parasite, Dendrosoter protuberans, imported from native haunts in Europe, is now well established in populations of its primary host, the smaller European elm bark beetle, in the Central States. In Missouri and Ohio, observed parasitism ranges from 25 to 40 percent. Three native parasites are commonly associated with the bark beetle, also. These natural enemies can be developed for use in an integrated control program to prevent Dutch elm disease buildup and spread.

TECHNOLOGY

Droplet Size Regulation. Spray generators have been developed to produce a narrow range of droplet sizes, and to capture and reclaim droplets of other sizes. This improves control of deposition on plants and reduces drift of fine droplets.

Granular Pesticide Dispenser. Dispensing of granular pesticides from hoppers can be made more uniform by design changes recently developed. Improvements in uniformity make it possible to reduce the total amount of pesticidal material required for effective pest control.

Insect-resistant Bags. The effectiveness of insect-resistant treated kraft/cotton laminated bags in protecting overseas shipments of food has been established.

Development of ULV - Short Boom Aerial Spray System. A new low cost versatile short-boom which can be installed and removed from any aircraft in less than two hours was successfully tested for ultra low volume (ULV) application against mosquitoes. This system should be very useful in emergency situations where large numbers of spray planes are needed to combat vector-borne diseases, epidemics, and insect outbreaks.

Ultra Low Volume Application. A safer yet effective pesticide application device has been developed to protect dairy animals from horn flies. The device employs the ultra-low-volume (ULV) technique and results in less quantity of pesticide required. Through use of this device and twice daily application horn flies were effectively controlled. The amount of pesticide required and correspondingly the amount of residue found in milk was reduced about a hundredfold.

New Adjustable Helicopter Spray System. A helicopter spray system for ultra-low volume application of microbial and chemical insecticides has been developed by Forest Service entomologists and engineers that allows changes in the rate of application from about 0.1 to 0.5 gallon per acre while in the air. Spray atomization remains constant if desired, or the spray spectrum can be altered by varying the spinning rate of the atomizing devices.

Careful Timing Reduces Number of Fungicide Treatments. In the Gulf States, weather favoring infection of pine nursery seedlings by fusiform rust is produced by high pressure systems. It is now possible to predict weather conditions favorable to rust infections 5 days in advance. By confining control efforts to these high-risk periods, rust losses in pine nurseries are minimized while pesticide use and costs are reduced.

New Control Methods Tested. Pilot control studies utilizing nonpersistent insecticides were conducted on 14,231 acres in Idaho and Washington. A new stabilized formulation of pyrethrum showed promise in controlling the hemlock looper. Zectran applied in very fine droplets failed to meet control criteria in suppressing the spruce budworm.

Systemic Insecticides Effective Against Cone Insects. Bidrin, Meta-Systox-R, Cygon, and Monitor applied at the rate of 5 grams active toxicant per inch of tree diameter reduced coneworm attacks in second-year slash pine cones by 80 to 90 percent. The Bidrin and Meta-Systox-R treatments reduced damage by another serious pest, the slash pine seedworm, by 95 percent. These materials are less toxic than others previously tested and found effective.

Cultural Treatment Is Improvement Over Chemical Brush Control. Following chemical brush control with 2,4-D, rabbit browsing is apt to be severe on Douglas-fir and other planted conifers. Oregon studies have indicated that where rabbits are prevalent, brush eradication by piling and burning instead of by chemicals should be considered.

Safer Rodenticide Under Test. A cooperative study is being conducted to test Diphacin as a substitute for sodium fluoroacetate to control seed-eating rodents prior to reforestation.

Improved Methods of Direct Seeding Reduces Pesticide Hazards. Previously mice and moles had been eating surface-sown seeds of white and red pine, even when coated with the rodent repellent endrin. Development of a mechanized seeder, which sows the seed and covers them with soil, resulted in very low seed losses to rodents. This makes direct seeding on rough lands practical even with very low levels of endrin. A reduced level of Arasan (1-1/2 percent) was also used on all seed in combination with the endrin.

Endrin-Arasan applications were tested to protect direct-seeded black walnuts from small mammals. Application directly to the nut, rather than to the soil proved more effective and introduced less endrin into the ecosystem.

Pest Management. Scouting programs will be inaugurated for selected crops in an attempt to reduce pesticide use by basing applications on pest counts rather than regular use for preventative control.

PESTICIDES AND MAN

G. A. Reich, M.D., M.P.H.

The Community Studies have been in operation for the past several years in 15 areas around the country carrying out prospective, epidemiological studies on persons occupationally exposed to pesticides. These persons have many times greater exposure to pesticides than does the general population; thus, it is to be expected that any adverse effect upon health which is due to pesticides would occur earlier and more widespread in this group. Also, if these persons over the years show no adverse effect, then it is reasonable to assume that the general population is in no greater danger. There are many problems and limitations to studying groups of people, especially when dealing with chemicals as ubiquitous and as numerous as pesticides.

Each Community Study has three basic components. The first is to determine the types and quantities of pesticide used in their area from season to season and year to year. Such data is necessary in order to comprehend the pattern of exposure to pesticides which the community experiences over any period of time. Obviously, any change in disease manifestation within the community must be examined in relation to qualitative and quantitative changes in pesticide exposure. The second component is the determination of the levels of certain organochlorine pesticides in human tissue. The purpose here is to determine the prevalence of these pesticides in the tissues of the general population of the community and to identify any secular trends. In addition, it is possible to examine changes in such levels with changes in disease manifestation, though there are certain epidemiological and statistical problems involved in this approach. Due to the characteristics of many pesticides, and due to the limitations in current analytical methods, only a few pesticides can be identified and quantitated in human tissue at the concentrations generally found in the general population. For the most part the pesticides usually found are (1) DDT and its metabolites; (2) the isomers of hexachlorocyclohexane; (3) dieldrin; (4) pentachlorophenol; and (5) heptachlor epoxide. Other compounds are found occasionally, and in cases of very high exposure with high tissue levels, numerous pesticides can be identified. The third component of each Community Study is a prospective study of workers occupationally exposed to pesticides. These workers receive an intensive clinical and biochemical evaluation of their health at least once a year. Detailed information of their pesticide exposure is collected periodically, while blood and urine specimens are obtained for analysis to identify certain pesticides and their metabolites.

The latter component is the main effort of the Program and may require 10, 15, or 20 years of continued observation to ascertain the adverse effects of this chemical exposure. Each of the studies has, in addition, several areas of special interest or special capability in medical research which develops data complementary to that of the overall program. One of these, common to all the studies, is the provision of diagnostic and therapeutic assistance in cases of acute pesticide poisoning. The purpose of this is two-fold: first to reduce the case-fatality ratio in cases of poisoning, and second to improve the reporting of poison cases, so that a more realistic figure for the actual incidence of such poisoning can be obtained. It is quite apparent that the incidence of acute pesticide poisoning varies a great deal from one area to another in the USA among the general population as well as the occupationally exposed workers. The two areas of highest incidence are in south Texas and in south Florida. In south Texas, pesticides are the leading cause of poisoning, running well ahead of aspirin, tranquilizers, etc. The cases of poisoning here have been, for the most part, among agricultural workers employed on farms and by spray pilots who are handling organophosphate pesticides. Their exposure is by the dermal route and due primarily to this, very few have died. In south Florida, pesticides are the leading cause of death by poisoning among children but rank only fourth or fifth among adult cases of poisoning. In this area, there are three manners of poisoning: (1) children who accidentally ingest pesticides in and around the home; (2) workers who are accidentally poisoned because of their occupational exposure; and (3) middle-aged to older adults who ingest pesticides with suicidal intent. Again, the organophosphates are the most important agents in poisoning. What follows now is a series of brief looks at some of the individual research of the various Community Studies.

The Arizona Community Study has carried out an experiment to clarify the way in which man metabolizes DDT. It has been well known that DDT is metabolized under anerobic conditions to DDD and under aerobic conditions to DDE. DDD, in turn, is metabolized to DDA, a water soluble end product which is excreted in urine. DDE, however, cannot be further handled by man and being lipid soluble is stored in adipose tissue. DDT, itself, being lipid soluble is also stored in adipose tissue. The first three figures depict these events in two persons, one taking 10 mg per day of DDT, and one taking 20 mg per day. Serum levels are presented in Figure 1 for DDE and DDD, adipose levels of DDE and DDD are presented in Figure 2, and the urinary excretion of DDA is presented in Figure 3. Levels of DDE continued to rise in adipose tissue even long after the feeding period had ended; however, in serum, only a small rise in DDE occurred, but it too continued after the feeding period had ended. DDE in serum is in equilibrium with DDE in adipose tissue, and both are influenced by the addition of new DDT and DDE and by the excretion of DDE. These data, though, suggest that levels of DDE in man may reflect primarily exposure to DDE per se rather than DDT as is currently the major opinion. DDE is probably the most ubiquitous of all pesticide related chemicals found in the environment. Though not shown on these figures, the serum and adipose levels of DDT rose sharply during the 6 months feeding period but then fell off sharply afterwards. The DDD levels in serum and fat had much the same pattern as DDT, since the major metabolic route in man is for DDT to go to DDD. DDA, the metabolite of DDD, had a pattern of urinary excretion similar to the serum and adipose levels of DDD. However, DDA excretion continues for months after the initial exposure; thus, it is quite useful in monitoring.

The California Community Study carried out a cytological examination of the sputum of workers occupationally exposed to pesticides. The results are presented in Table 1. Four of the five characteristics had essentially similar prevalence, but metaplasia was significantly more frequent among the pesticide workers. Figure 4 shows how this 43% prevalence of squamous metaplasia stacks up against other occupational groups. Cigarette smokers with a known significant risk of lung cancer have a prevalence of 24%, while the group "urban traffic fumes" which represents police directing traffic has a prevalence of 37%. This is not to say that merely because squamous metaplasia is present, lung cancer or emphysema will develop. What it indicates is that this pathological sign is present in a significant number of people, and now these people must be followed over time to determine what proportion of them develop lung cancer and other pulmonary disease.

A very important observation made by the California Community Study has been of the importance of the skin as a route of exposure for pesticides. Pesticides appear to have differences in dermal absorption in man. Table 2 depicts some of these when applied to the forearm. Minor damage to the skin as produced by "stripping" increased absorption by 4 to 10 fold. Stripping is done by applying scotch tape to the skin and then yanking it off. This removes some of the outer, cornified cells of the skin. Abrasions which expose the deeper layer, the dermis, are already known to greatly enhance absorption as do acute and chronic skin conditions. Occlusion of the skin with a covering also increases absorption 4 to 10 fold; this is important to persons who wear contaminated gear or clothing while handling pesticides. Also, it was noted that blacks absorb 25% to 50% more pesticides than do whites under the same conditions of exposure. The site on the skin where exposure occurs is of considerable importance. Using parathion as an example, Table 3 indicates a variation from 9% to 100% as the site varies from forearm to scrotum.

The Colorado Community Study has carried out studies of persons in the family setting and determined the importance of environmental levels in the exposure which the family receives. The data indicate a highly significant correlation between levels of pesticides in house dust and levels of pesticides in the blood of the family. This correlation suggests that one's immediate environment may be more important a source of pesticide exposure than food. Confirmatory work has been carried in Utah and is reviewed ibid.

The Florida Community Study has looked into the aspect of chemical interaction in the metabolism of pesticides and drugs. Certain drugs like phenobarbital, but especially diphenylhydantoin (Dilantin), greatly increase the metabolic breakdown of DDT in man. This leads to significantly lower tissue levels in man. The mechanism for this is probably the induction of liver microsomal enzymes. It has also been shown that drugs which are hepatotoxic(like coumadin) have the opposite effect, and by interfering with DDT metabolism lead to higher tissue levels. Similarly in states of malnutrition such as scurvy, the metabolism of pesticides is quite slow and inefficient.

Data from the Florida Community Study and the Monitoring Program of State Services Branch of this Program indicate that there are racial differences in the tissue concentrations of certain pesticides, the blacks having significantly higher concentrations. Also, persons living in the South have higher concentrations than those in the North. Males tend to have higher concentrations than females, especially among blacks. This suggests that several factors are at play in determining one's concentration of pesticides.

The Florida Community Study has also observed that the organochlorine pesticides cross the placenta. This occurs in a ratio of about one to two or one to three. No health risk is yet apparent, though premature infants have significantly higher levels of DDT and DDE than full term infants.

The Hawaii Community Study follows a variety of persons occupationally exposed to pesticides. Pesticide exposure is a highly variable characteristic in both a qualitative and quantitative sense. The mean serum levels of certain pesticides are shown for three exposed groups and a control group in Table 4. DDT, dieldrin, and pentachlorophenol exposure is quite different for these groups. These differences in exposure are important aspects to consider when adverse health effects are detected. Similarly, differences in health status must be judged very critically. A statistical way of looking for relationships between certain pesticides and certain biochemical functions is demonstrated in Table 5. These are the results of a stepwise multiple regression analysis wherein numerous factors can be handled simultaneously.

There are various classes of chemicals which are clearly mutagenic. Certain pesticides fall in these classes: alkylating agents, radical producing agents, etc. Hawaii is now carrying out an investigation into mutagenesis by the use of dermatoglyphics; these data are complementary to those to be mentioned in connection with the Michigan Community Study. Of equal importance in studying the health effect of chemicals is the subject of teratogenesis. Such a study is now underway in Hawaii utilizing vital statistics. Perhaps the three characteristics of chemicals which are of the greatest public health concern are: carcinogenesis, mutagenesis, and teratogenesis. Determining whether or not such effects are occurring in man is a difficult but important task for the Community Studies.

The Idaho Community Study has carried out a study of chromosomal aberrations in workers employed in a captan formulating plant and to date, have not found chromosomal damage. Recently, the Study did discover that the pheasants in the state were contaminated with mercury. This was at about the same time that Canada discovered its pheasant to be contaminated with mercury. These environmental contaminations are important considerations in public health for two reasons: (1) many of the plants and animals involved wind up in the human food chain and may pose a threat due to biological concentration; and (2) situations giving rise to contamination of wildlife or domestic animals may signal human contamination as well; e.g., Minimata Disease.

Idaho has been conducting extensive neurological evaluations of persons exposed to pesticides and has observed in cases of mild poisoning that the EEG resembles that seen in temporal lobe epilepsy.

The Iowa Community Study is located in the corn belt and has been studying primarily farmers. Utilizing extensive biochemical evaluation an interesting observation was noted regarding variations in certain biochemical functions. Table 6 demonstrates LDH activity in the pesticide exposed farmers as compared with controls off-season and on-season. The LDH activity declines significantly in the exposed group during the pesticide use season; however, LDH activity also declines significantly among the controls. This suggests that there is a marked seasonal variation in LDH activity inherent in all men, or perhaps that due to the flat topography of Iowa and the usual wind, no one escapes pesticide exposure during the high-use season.

Due to a study being conducted in relation to organophosphate exposure and the use of succinyl choline during anesthesia, it was noted that certain persons have an atypical cholinesterase activity because of genetic variation. Figure 5 shows a pedigree for this, and points out that it is transmitted as a homozygous or heterozygous state by normal Mendelian laws. This variation increases one's susceptibility to the acute, toxic effects of organophosphate pesticides.

Behavioral and neurophysiological studies in sheep have been underway for several years determining the effect of dieldrin, ruelene, and DDT. Continuous monitoring of the sheep's EEG demonstrated major changes in brain wave patterns. Correlations between these EEG changes and decrements in behavioral performance were noted with all three pesticides. With some, performance gradually returned to normal even with continued exposure; however, the performance of others improved only some time after discontinuance of exposure or not at all.

The Michigan Community Study has been conducting a longitudinal survey of chromosomal aberrations utilizing cell cultures from peripheral blood. The purpose here is to compare the frequency of chromosomal aberrations among the exposed group to that of the control group to determine if there are significant differences in the incidence of this phenomenon. One expects that the control group will have chromosomal aberrations, because everyone is exposed to chemical and physical agents known to be mutagenic. The question is, "Do those exposed to pesticides have a significantly greater incidence of chromosomal aberrations than the general population?" Table 7 presents the results of this survey over five consecutive months. The sorts of chromosomal changes looked for are: (1) a numerical change; or (2) a structural change. Numerical changes are aneuploidy, polyploidy, and mitotic index. Aneuploidy is a difference in chromosome number, polyploidy is the presence of two or more complete sets of chromosomes, and mitotic index is the ratio of dividing to non-dividing cells. Structural changes are deletion and exchange, and both vary quantitatively. What was observed among the pesticide workers were breaks in the chromosomes; there was some increase in aneuploidy but this was not statistically significant.

Such mutational effects are very important in public health, because of the question of cancer and, or course, the transmission of genetic change to the next generation. Determining whether or not this risk is real requires the continued observation of these persons.

The Mississippi Community Study is located in the area of greatest pesticide use in the country. Table 8 depicts the types and quantities used in just a three county area from 1967 to 1969. Air monitoring activities indicate considerable use. This pattern of current use is expected to change as the persistent pesticides are increasingly restricted, and users then turn to organophosphates and carbamates. The delta area of Mississippi and of Arkansas accounts for a considerable portion of crashes of aerial applicators. This reflects the significance of aerial application in cotton raising in this area and indicates the hazard of these chemicals to pilots. The conditions under which these pilots fly do not allow for minor aberrations of reaction time, coordination, vision, etc. which can be produced by mild exposure to pesticides.

The New Jersey Community Study has the largest number of workers under observation of any of the Studies. These men are employed in manufacturing and formulating plants. Table 9 gives an indication of the sorts of biochemical tests done on these workers. The different plants represent different pesticides for the most part; so this area, in contrast with many of the other Studies, has workers exposed to only one or a few pesticides, thus making the job of identifying the more hazardous pesticides easier. New Jersey also carries out an extensive state-wide program to assist in the diagnosis, treatment, and reporting of acute pesticide poisoning. One episode investigated involved three cases of acute poisoning with arsine gas wherein the workers put an aluminum ladder in a tank in which an organoarsenical was being manufactured. Usage of a wooden ladder would not have given rise to a problem.

The South Carolina Community Study carried out an ophthalmological study of 30 people using echothiophate iodide eye drops for the treatment of glaucoma or accomodative esotropia. This organophosphate eye solution was only 0.25%, but gave rise to systemic effects as indicated by declining red cell and plasma cholinesterase activity.

The Texas Community Study is located in a region of intensive use, especially ULV application by plane. This region has experienced episodes of acute pesticide poisoning due to organophosphates. DDT dropped out of use some years ago in this area, but the exposed population still retains high blood levels of DDE. Some formulators still retain high blood levels of DDT, β-BHC, and dieldrin. Table 10 shows some tissue levels of certain pesticides from the general population obtained by various investigators.

The Utah Community Study has looked into the relative importance of food and house dust levels of pesticides in predicting blood levels of pesticides. Levels in house dust were considerably higher than in food. The correlation between food and blood levels was $r=0.39$, indicating that about 15% of the variation in blood levels is due to food. The correlation between house dust and blood levels was $r=0.48$, indicating that about 23% of the variation is due to house dust. This points out the importance of considering the other sources of pesticide exposure in addition to food. The relative importance of any particular source depends upon the contamination of that source and the frequency with which one is in contact with it.

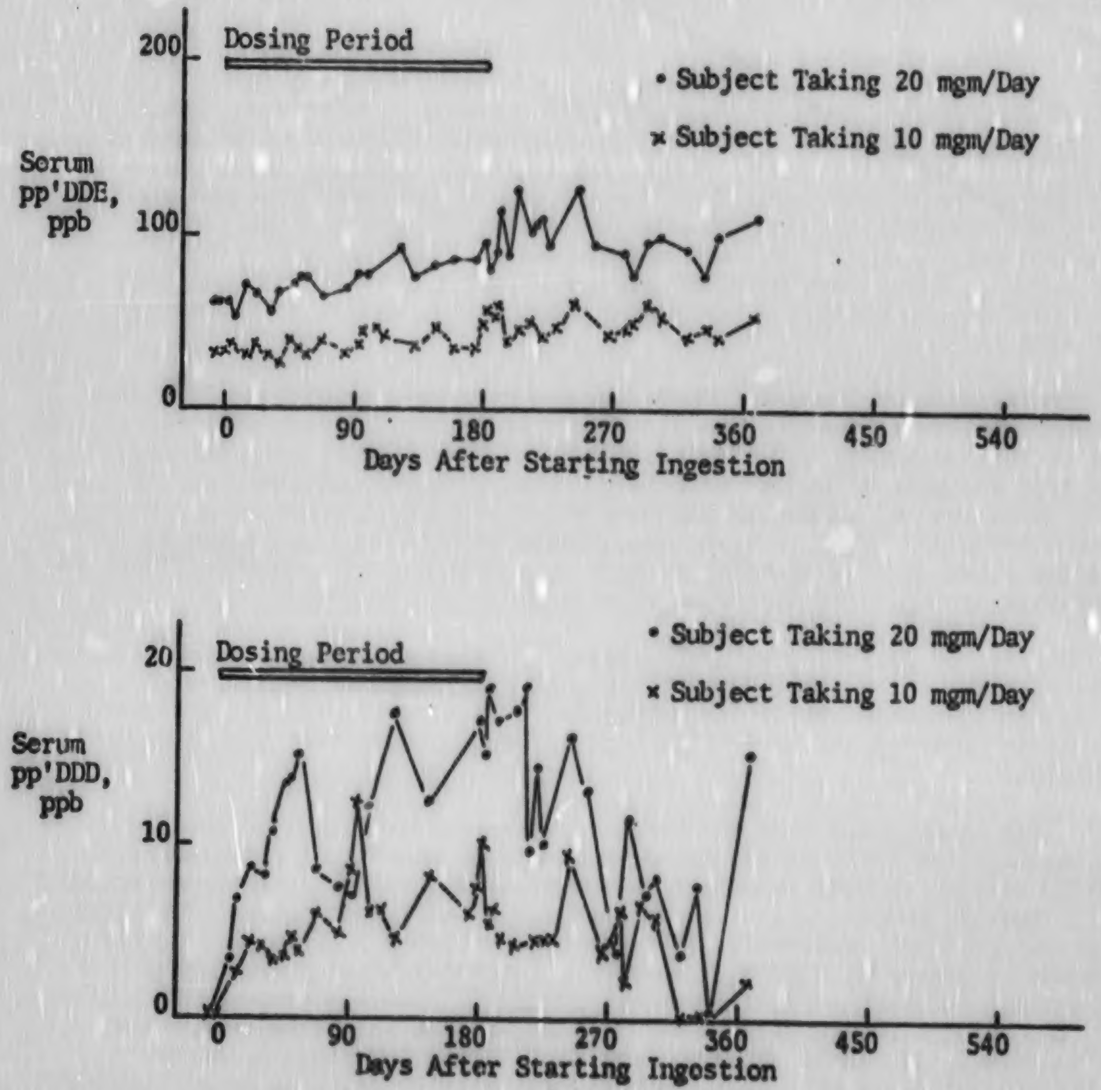
The Washington Community Study has analyzed test results in a fashion somewhat similar to that in Hawaii. Table 11 depicts certain biochemical test results as they appear to be influenced by different types of pesticides. This type analysis helps to indicate the site of action of these pesticides in humans and suggests where one might look for heretofore undiscovered pathology. On the other hand, these changes must be looked at from the point of view of being perhaps only adaptive in nature and thus reversible upon discontinuance of exposure.

Pooling of data from all the studies has allowed us to more critically examine the clinical data of the program. Table 12 demonstrates the season to season results race-specific. These differences are between those who are occupationally exposed and controls from the general population.

These comparisons show no obvious differences except blood DDT and DDE levels. The clinical indices demonstrate no consistent differences. Pooling of data is very important to the program. In any research oriented public health program, there is the need for a sufficient number of persons under observation. Presently, this can be approached only by pooling data from the 14 Community Studies. Many more Community Studies are needed.

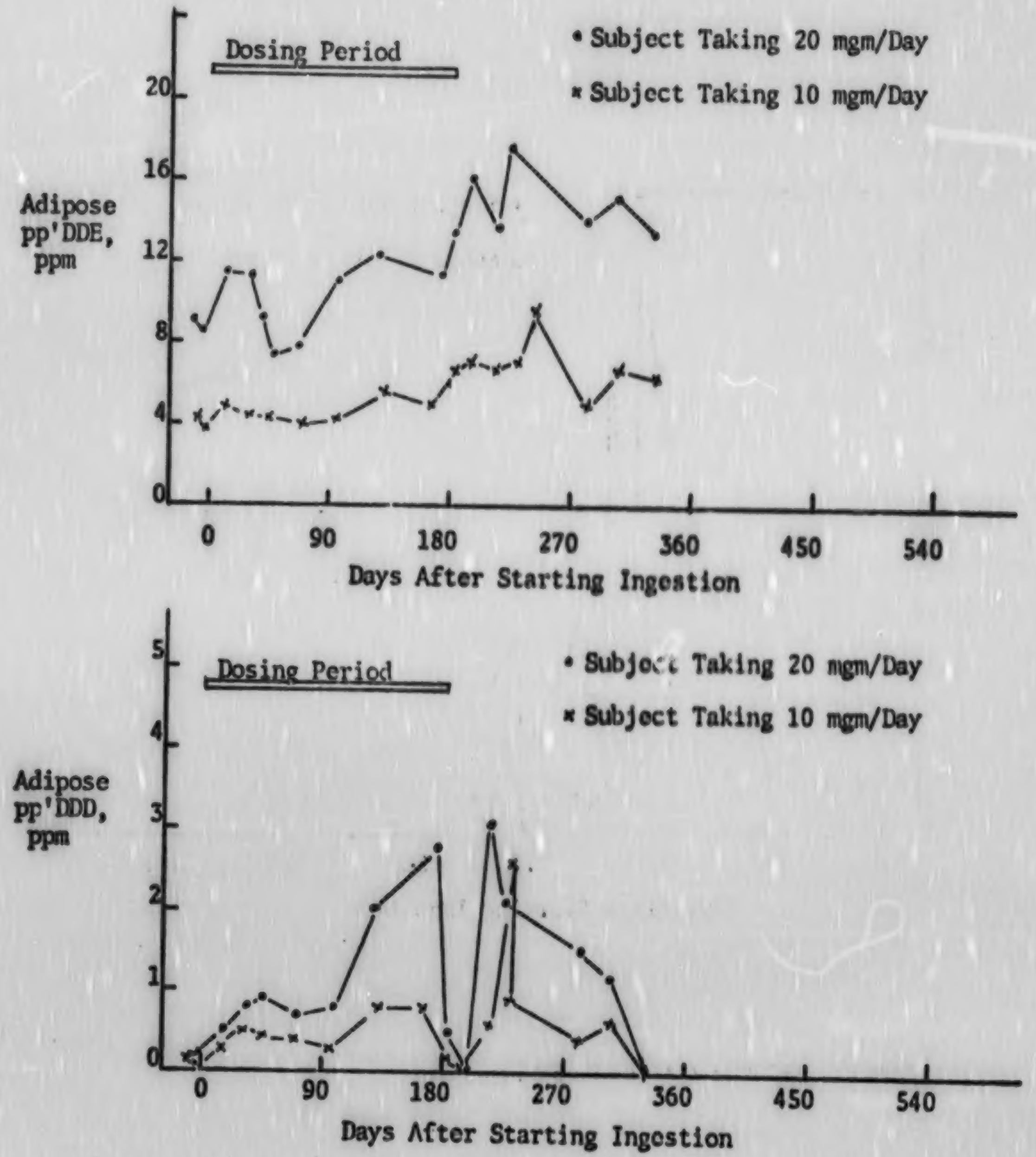
One thing is quite clear. It is going to take some time before the health effects of pesticides are understood in a comprehensive manner. It is also quite probable that these effects will be found to be an integral part of the overall effect which chemical contamination of the environment has upon the health of the populace. The presence of on-going Community Studies which monitor the health status of segments of the population can serve as the early warning device for detecting qualitative or quantitative changes in mortality and morbidity patterns in the country.

FIGURE 1
CHANGES IN SERUM LEVELS OF pp'DDE AND
pp'DDD IN 2 SUBJECTS INGESTING 10 AND
20 mgm PER DAY TECHNICAL DDT FOR 6 MONTHS.



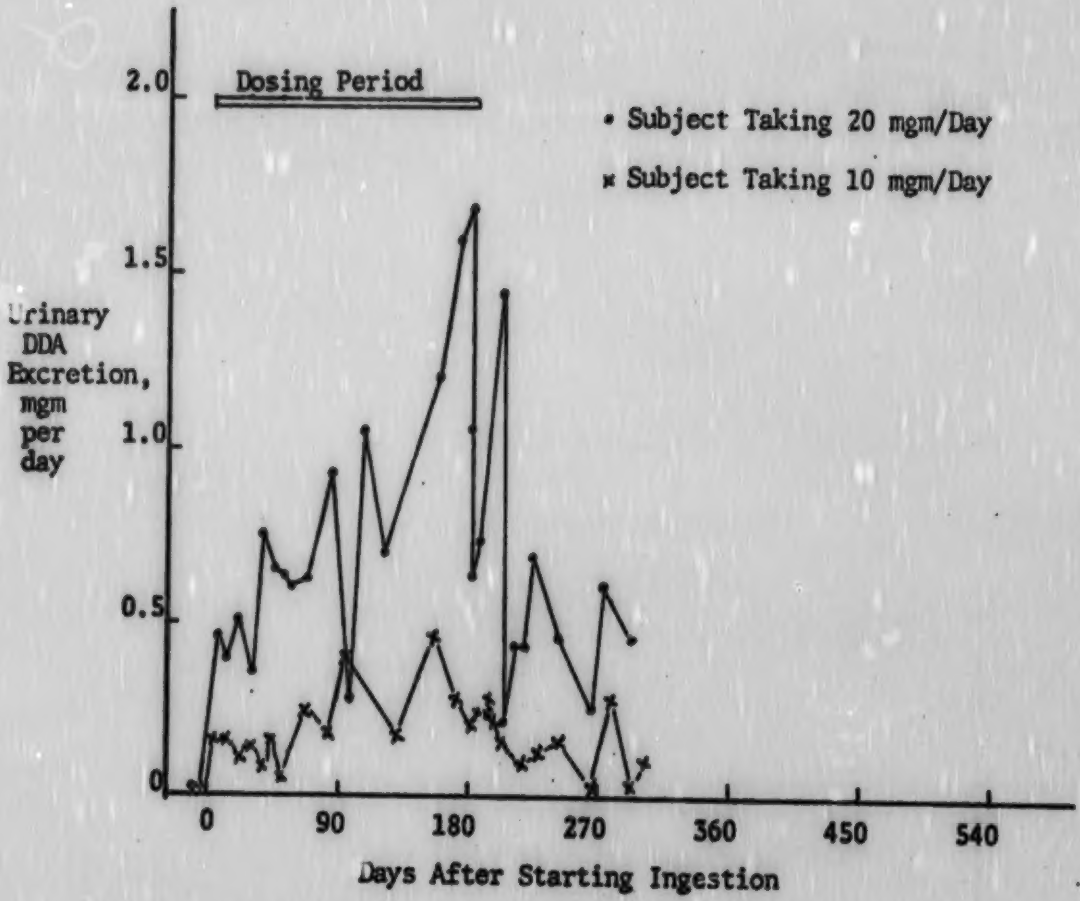
SOURCE: ARIZONA COMMUNITY STUDY

FIGURE 2
CHANGES IN ADIPOSE pp'DDE and pp'DDD
CAUSED BY INCREASING DIETARY INTAKE OF
TECHNICAL DDT BY 10 and 20 mgm PER DAY
FOR 6 MONTHS IN 2 SUBJECTS



SOURCE: ARIZONA COMMUNITY STUDY

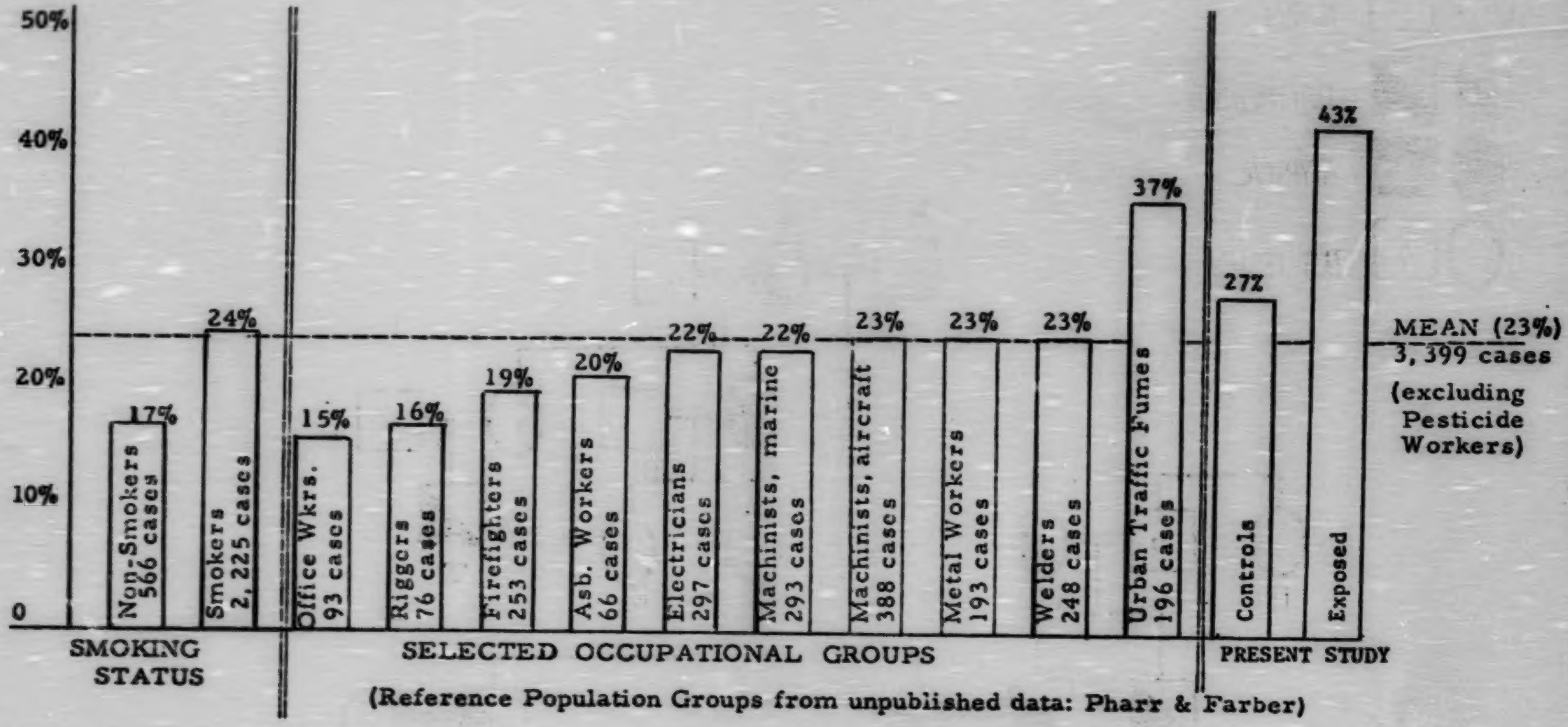
FIGURE 3
CHANGES IN URINARY DDA EXCRETION
CAUSED BY INCREASING DIETARY INTAKE OF
TECHNICAL DDT BY 10 and 20 mgm PER DAY
FOR 6 MONTHS IN 2 SUBJECTS



SOURCE: ARIZONA COMMUNITY STUDY

Figure 4

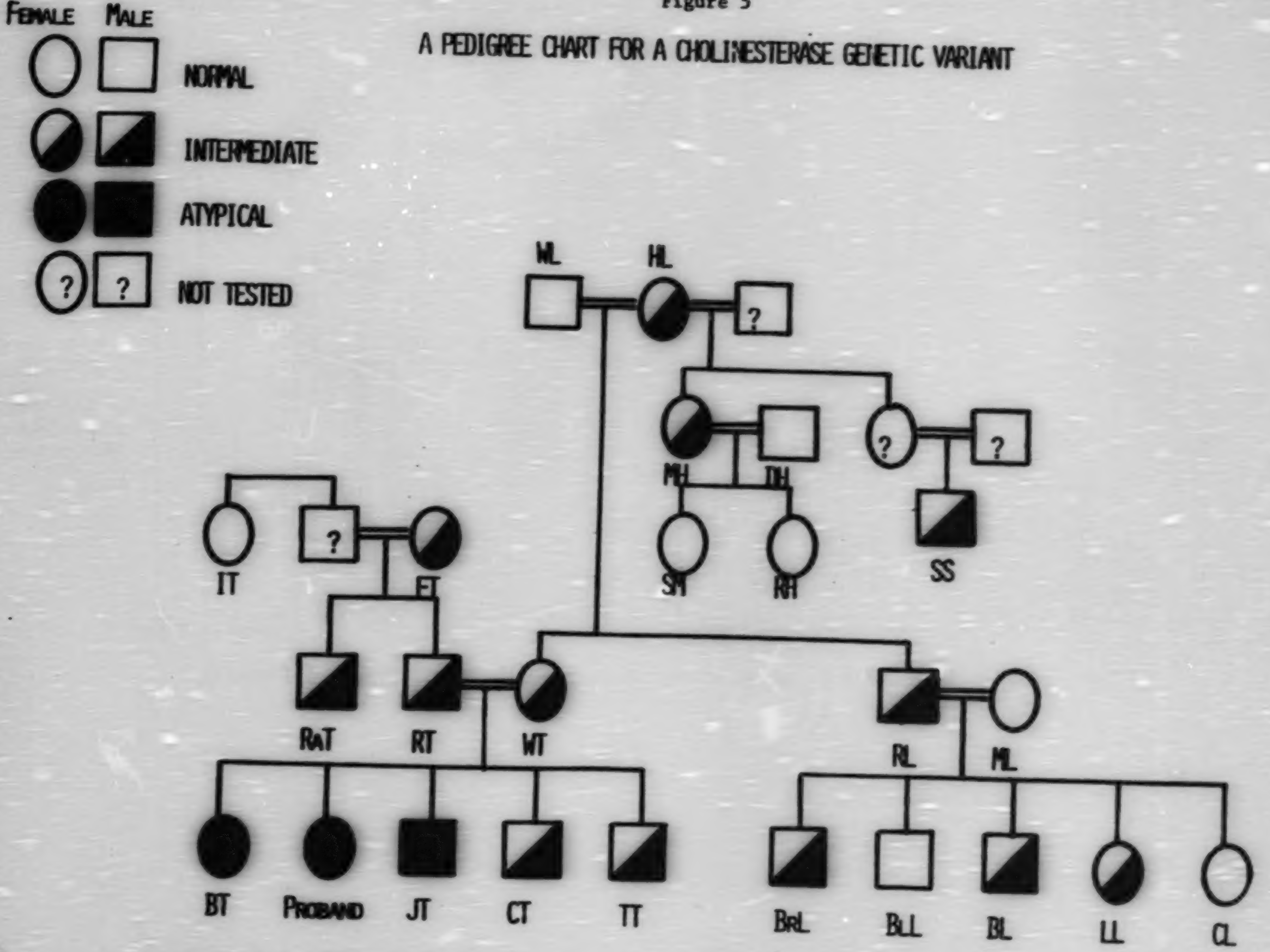
METAPLASIA : PREVALENCE IN SPUTUM AMONG SELECTED POPULATION GROUPS



SOURCE: CALIFORNIA COMMUNITY STUDY

Figure 5

A PEDIGREE CHART FOR A CHOLINESTERASE GENETIC VARIANT


FEMALE
MALE
NORMAL
INTERMEDIATE
ATYPICAL
?
?
NOT TESTED
WL
HL
?
MH
DH
?
?
SM
RH
SS
IT
?
FT
RaT
RT
WT
RL
ML
BT
PROBAND
JT
CT
TT
BrL
BLL
BL
LL
CL

SOURCE: IOWA COMMUNITY STUDY

Table 1

Characteristics	Percent Showing	
	Controls n=419	Exposed n=1,362
Inflammation	40%	36%
Irritation	29%	29%
Allergy	9%	8%
Obstruction	12%	9%
Metaplasia	27%	43%

SOURCE: CALIFORNIA COMMUNITY STUDY

TABLE 2

DIFFERENCES IN THE DERMAL ABSORPTION OF PESTICIDES

PESTICIDE	PER CENT ABSORBED
Thiourea	<1
Diquat	<1
2,4-D	6
Malathion	7
Dieldrin	8
Parathion	9
Lindane	9
DDT	14
Baygon	20
Sevin	75

SOURCE: CALIFORNIA COMMUNITY STUDY

TABLE 3

DIFFERENCES IN AMOUNT OF PESTICIDE* ABSORBED BY SITE OF APPLICATION

SITE OF APPLICATION	PER CENT ABSORBED
Forearm	9
Palm	12
Abdomen	19
Back of Hand	21
Antecubital Fossa	29
Scalp	32
Back of Ear	34
Forehead	36
Ear Canal	47
Axilla	64
Scrotum	100

*=Parathion

SOURCE: CALIFORNIA COMMUNITY STUDY

TABLE 4

MEAN SERUM LEVELS OF ORGANOCHLORINES AMONG CONTROLS AND EXPOSED IN HAWAII

ORGANOCHLORINE	OCCUPATIONAL GROUPS			
	CONTROLS	ORGANOCHLORINE	ORGANOPHOSPHATE	PCP[1]
P,P' DDT	4.59	8.29	6.73	2.62*
P,P' DDE	20.82	21.76	21.02	12.39
Dieldrin	1.65	38.81	2.35	1.31*
β BHC	1.0	1.0	1.27	0.39
PCP[1]	.19	1.08	0.65	6.06*

SOURCE: HAWAII COMMUNITY STUDY

*Significant difference between occupational groups.
[1] = Pentachlorophenol

TABLE 5

Physical and blood biochem. variables	Rac. Extr.	Males a/ p,p' DDT	Males a/ p,p' DDE	Males a/ Dield.	Males a/ α BHC	Males a/ β BHC	Males a/ γ BHC	Males a/ Hep. epox.	Females b/ p,p' DDT	Females b/ p,p' DDE	Females b/ Dield.	Females b/ α BHC	Females b/ β BHC	Females b/ γ BHC	Females b/ Hep. epox.
Blood glucose	Cauc.	.1317	.0225	.0032					.0122						
	Jap.			.0058											
	Other	.0173	.0605						.0038					.0013	
B U N	Cauc.		-.1738												
	Jap.						-.0001								
	Other		-.2953	-.0158					.0984	.3148				.0001	
Uric acid	Cauc.											.8488			
	Jap.			.1946			.2318								
	Other	-.5256		.0811					.2289						
Cholesterol	Cauc.														
	Jap.			.0036			-.0032								
	Other		.0497	.0016						.0181	.0019			-.0013	
Calcium	Cauc.								1.099						
	Jap.						.6821								
	Other		-2.507	.2067					-.5813					-.3247	
Total protein	Cauc								-1.314		.5817				
	Jap.														
	Other									-2.853				-.0004	
Albumin	Cauc.								1.441	3.082	.4736				
	Jap.														
	Other		-3.824	.3332					-.8081	7.797			.2872	.0002	
Bilirubin	Cauc.								-4.533	- 9.45	-2.088	-5.108			
	Jap.														
	Other		-8.475	.6713									-.5546	-.0001	

a/ 321 males divided into 167 Caucasian, 79 Japanese & 75 others
b/ 245 females divided into 118 Caucasian, 61 Japanese & 66 others
c/ only significant coefficients are given (P<0.05) ; their absolute magnitude cannot be used for ranking purposes

SOURCE: HAWAII COMMUNITY STUDY

TABLE 6

CHANGES IN MEAN LDH VALUES BY SEASON AND EXPOSURE STATUS

	SEASON 1	SEASON 2	S1 - S2
Low Exposure	357.6	294.4	63.2*
High Exposure	340.3	252.0	88.3*
Low - High	17.3ns	42.4*	

ns = not statistically significant
* = significant

ADDITIVE EFFECT OF SEASON AND EXPOSURE STATUS ON MEAN LDH CHANGES

	S1 - S2		Low Exposure - High Exposure
Low Exposure	63.2	S1	17.3
High Exposure	88.3	S2	42.4
Total	151.5	Total	59.7
$\bar{x}$	75.75	$\bar{x}$	29.85

$\bar{x}$ S1-S2/$\bar{x}$ Low Exposure-High Exposure = 2.54

SOURCE: IOWA COMMUNITY STUDY

TABLE 7

LYMPHOCYTE CHROMOSOME ABERRATIONS 1969
NUMBER OF CELLS WITH DAMAGE/NUMBER OF CELLS EXAMINED

	CONTROL	EXPOSED
June	4/258	10/616
July	2/597	11/600
August	7/225	8/330
September	1/294	6/497
October	5/229	5/298
TOTAL	19/1603	40/2341

SOURCE: MICHIGAN COMMUNITY STUDY

TABLE 8

ESTIMATED PESTICIDES USED ON ALL MAJOR CROPS IN 1967, 1968, and 1969

PESTICIDE	POUNDS OF TECHNICAL MATERIAL		
	1967	1968	1969
INSECTICIDES			
TOXAPHENE	840,000	1,600,000	2,961,000
DDT	536,000	1,035,800	2,473,250
STROBANE	62,400	112,000	100,000
TDE	48,000	121,600	305,000
ENDRIN	43,600	36,860	20,000
KELTHANE	15,000	15,000	15,000
METHYLPARATHION	316,000	509,700	1,634,500
GUTHION	31,840	67,200	37,500
AZODRIN	27,600	25,800	118,000
BIDRIN	21,640	11,800	35,000
DISYSTON	15,900	12,900	19,100
THIMET	7,500	9,300	20,500
MALATHION	6,500	3,000	15,000
SEVIN	15,375	10,500	42,300
HERBICIDES			
TREFLAN	344,200	226,000	320,000
MSMA	300,700	342,000	534,000
DALAPON	167,570	54,000	120,600
PROPANIL	106,309	123,800	191,000
LOROX	93,000	60,000	79,000
KARMEX	77,800	52,500	83,000
PLANAVIN	76,100	208,000	75,000
HERBAN	44,800	40,000	57,000
VERNAM	40,000	15,000	5,000
COTORAN	36,800	76,500	154,000
2,4,5-T	25,305	22,400	56,000
DSMA	21,600	27,500	5,000
TELVAR	14,000	58,200	24,200
AMIBEN	9,600	0	77,100
CAPORAL	3,520	4,000	9,500
SILVEX	2,736	1,800	100
EPTAM	560	400	400
DINITROPHENOL	0	35,000	50,000
TENORAN	0	24,000	36,000
2,4-D	0	4,500	4,500
PARAQUAT	0	500	1,000
DEFOLIANTS			
SODIUM CHLORATE	186,680	356,000	375,000
DEF/FOLEX	112,200	225,000	220,000

SOURCE: MISSISSIPPI COMMUNITY STUDY

TABLE 9

Biochemistry (SMA-12)
Number of Abnormal Tests* and Number of Individuals with Abnormal Tests**

	# of Tests	#of Indi-viduals Tested	GLU	BUN	Uric	Chol.	Ca	Phos.	T.Bi.	Alb.	TP	A/G	LDH	A.PH	SGOT	SGPT	CPK	Creat.
Plant A	29	19	6/6	17/14	1/1	5/3	2/2	3/3	3/3	4/4	3/3	6/5	8/8	4/4	8/7	2/2	2/2	0/0
Plant C	70	19	23/14	13/7	5/4	6/3	3/3	6/5	5/4	4/4	6/6	9/8	18/13	14/6	17/14	2/2	6/5	3/3
Plant D	25	11	5/5	5/3	5/3	0/0	0/0	4/2	1/1	1/1	1/1	5/4	5/3	7/4	14/10	0/0	1/1	1/1
Plant E	117	77	22/19	14/13	19/16	12/11	18/17	10/10	4/4	19/19	10/9	17/14	40/36	9/9	28/24	4/4	9/9	12/12
Plant F	14	6	4/3	0/0	2/2	4/2	2/2	4/2	0/0	4/2	4/2	6/3	6/4	0/0	0/0	0/0	0/0	0/0
Plant H	30	13	9/8	1/1	9/4	4/4	3/3	5/4	3/3	7/6	3/1	5/4	6/5	0/0	10/8	1/1	6/5	3/3
Plant L	12	7	1/1	0/0	7/5	0/0	2/2	1/1	0/0	1/1	2/2	4/3	1/1	3/3	5/5	1/1	2/2	
Controls	88	48	23/21	17/14	13/11	1/1	6/5	26/22	6/5	7/6	6/6	30/23	23/20	6/6	23/21	0/0	0/0	0/0

SOURCE: NEW JERSEY COMMUNITY STUDY

*Numerators
**Denominators

Table 10

COMPARATIVE ORGANOCHLORINE RESIDUE LEVELS** IN ADIPOSE TISSUE OF DIFFERENT POPULATIONS

Study Population	Year	pp'DDT	pp'DDE	op'DDT	pp'DDD	B-BHC	Dieldrin	Hept.Epoxide	Reference
282 Autopsies, Chicago	1962-1963	2.4*	6.1*			0.4*	<.05*		Hoffman
28 surgical biopsies, Wenatchee, Louisville, Phoenix, Atlanta	1961-1962					0.20	0.15		Dale et Quinby
64 Autopsies, Northwest, Far West, South, Midwest	1964	2.35	4.63	0.16			0.31	0.10	Zavon
159 Autopsies, Dade County, Fla.	1965-1967	White+ 3.0 Nonwhite 7.1	White* 4.9 Nonwhite* 9.6				0.22		Davies, Edmundson
25 Autopsies, New Orleans	1964	1.73	6.85	.06	.45	0.60	0.29	0.24	Hayes
44 surgical biopsies Great Britain	1964						0.22*		Robinson & Hunter
31 surgical biopsies Rio Grande Valley	1969	1.8*	7.8*	0.23*	0.06*	0.51*	0.22*	0.07*	present communication

** All results expressed in ppm; analyzed by gas chromatography

* Median values (all others are means)

+ Calculated values: median total DDT derived material minus median pp' DDE

SOURCE: TEXAS COMMUNITY STUDY

TABLE 11

SIGNIFICANT F TESTS (α=.05) OF BIOCHEMICAL VARIABLES AGAINST QUARTILES OF RED CELL CHOLINESTERASE INHIBITION AND QUARTILES OF SERUM LEVELS OF p,p'DDE

TEST	INDEX OF EXPOSURE	
	Red Cell ChE	DDE
SGOT	+	+
Uric Acid	+	-
Albumin	+	-
γ-Globulin	+	-
Total Protein	+	-
Red Cell Count	+	-
Urine P	+	-
Cholesterol	-	+
Alkaline Phosphate	-	+
BUN	-	+
Plasma Thromboplastin Time	-	+

+ = significant at 5% or better
- = not significant

SOURCE: WASHINGTON COMMUNITY STUDY

TABLE 12

POOLED DATA COMPARISONS
RACE SPECIFIC

VARIABLE	WHITE[1]				BLACK[2]			
p,p' DDT	+[3]	+	+	+	+	+	+	+
p,p' DDE	+	+	+	+	+	+	0	+
β-BHC	0	+	+	+	+	+	0	0
Dieldrin	0	+	+	+	0	+	0	+
Red Cell ChE	0	+	0	0	0	-	-	0
Plasma ChE	-	-	0	0	0	-	-	0
Serum Creatinine	+	+	0	0	-	0	-	0
FBS	0	0	0	0	+	0	0	0
Total Protein	0	0	0	0	+	-	-	0
α_1 Globulin	0	0	0	0	0	0	+	0
α_2 Globulin	0	0	0	0	0	0	0	0
β-Globulin	0	0	+	-	0	0	-	0
γ-Globulin	0	0	0	0	0	0	0	0
Albumin	0	0	0	+	-	0	-	0
Uric Acid	0	0	0	0	0	-	-	0
Total Bilirubin	-	0	0	-		0	-	-
Cholesterol	0	0	0	0	0	0	0	0
Hematocrit	0	0	+	0	0	0	0	+
Hemoglobin	0	0	0	0	0	0	0	0
WBC	0	0	0	0	0	0	0	0
Urine pH	0	0	0	0	0	+	0	0
BUN	0	0	0	0	0	0	0	0

[1] = Number of controls varies from 58 to 239; number of exposed from 77 to 504
[2] = Controls vary from 9 to 70; exposed from 26 to 163
[3] = Each column reflects one season
+ = Exposed results significantly (α=.05) greater than controls
- = Vice Versa
0 = No significant difference
Blank = Inadequate data

TERATOLOGY AND MUTAGENICITY OF PESTICIDES

Clara H. Williams, Ph.D.

1. Teratology

The science of experimental mammalian teratology began in the 1930's, although experiments on teratology of the lower classes of animals such as birds and amphibia had been in progress for nearly one hundred years. Job, Leibold, and Fitzmaurice (1935) produced malformations in the young of rats which had been exposed to X-rays.

In 1933 Hale produced congenital malformations in pigs by creating a Vitamin A deficiency in the sows.

The famous thalidomide disaster of the early 1960's accelerated the interest in the teratology of drugs. In 1968 the so-called "Bionetics" screening study which investigated the teratogenic potential of a number of widely used pesticides stimulated investigations in this area. In 1969-70 discovery of high levels of methyl mercury in fish of the American rivers, bays, and lakes spurred interest in the teratogenic effects of this compound. The Japanese had had this problem during the years of 1953-58 (Minimata Bay disease) and in 1964-65 (Niigata disease).

The teratology of pesticides has been very little explored. One reason for this is that the normal exposure of humans to pesticides is at a very low level over extended periods, while the drugs are administered usually acutely or subacutely in known amounts. Because of time limitations the present discussion will consider only teratology in placental mammals. Avian teratology presents difficulties in attempting to extrapolate safety to man, since the avian embryo is non-placental.

In testing for the teratogenic potential of a compound, there are five important factors to consider: (1) the period of administration, (2) the route of administration, (3) the size of the dose, (4) the species used, and (5) the presence of additional stress.

The interpretation of what constitutes true terata is a subject of considerable disagreement among investigators. One interesting aspect of teratogenesis is the lack of specificity for any one organ. A spectrum of congenital malformations can appear in one species from one compound.

The most recent interest in investigating the teratogenesis of pesticides was actually derived from a study made by the National Cancer Institute through the Bionetics Research Laboratories of the Litton Industries. In 1965 this laboratory screened a number of pesticides for possible teratogenic activity in several strains of mice. The following 12 pesticides showed an increase in the number of anomalies in the live fetuses when tested in a C57/Bl strain of black mice: 2,4,5-T, PCNB, captan, folpet, isooctyl-, butyl-, isopropyl-, methyl-esters of 2,4-D, carbaryl, IPC, and carbaryl + piperonyl butoxide. 2,4-D itself showed an increased number of anomalies in the AKR strain of mice but not the C57/Bl strain.

After the Bionetics report appeared, interest was focused upon 2,4,5-T because of its wide use as a defoliant by the military services in Vietnam. Courtney (1970a) found that 2,4,5-T was teratogenic and feticidal in two strains of mice when administered either subcutaneously or orally and in one strain of rats when administered orally. It was found, however, that the Courtney sample of 2,4,5-T contained 30 ppm of 2,3,7,8-tetrachlorodibenzo-p-dioxin. At about the same time evidence was accumulating that this dioxin was highly embryotoxic and teratogenic (Sparschu, 1970). Collins (1970) at FDA using hamsters as a test animal tested 2,4,5-T from several commercial sources and found that as the dioxin content of the 2,4,5-T increased the fetal toxicity increased but 2,4,5-T alone produced some fetal anomalies.

2,4-D and many of its esters are also widely used. As was mentioned before, the esters of 2,4-D proved to be teratogenic in the C57 mice but not the 2,4-D free acid. The acid was, however, teratogenic in the AKR strain of mouse. Collins (1970) using Golden hamsters studied the teratogenicity of 2,4-D acid from several commercial sources. Although the number of terata in the hamster fetuses in some instances was increased over that of the controls at the 100 mg/kg dose, this dose is in excess of normal exposure to allowable levels of this herbicide.

The toxicity and teratogenicity of mercury containing compounds have become a world-wide issue. Various alkyl mercury compounds have been used as fungicides for seed coatings. Mercury salts have become accidental environmental contaminants because of the dumping into the streams, rivers, and lakes by industrial plants of elemental mercury which is converted to methyl mercury by microorganisms. The teratogenic properties of methyl mercury are of interest because this form of mercury appears to have a greater affinity for fetal brain tissue than maternal brain tissue.

Nonaka (1969) produced experimental Minimata disease in the young of rats dosed with methyl mercury chloride.

At FDA, Collins et al. studied teratogenic properties of methyl mercury chloride in hamsters and rats. A dose-related incidence in the number of terata was found, but the incidence of embryotoxicity did not appear to be dose-related. In both the rat and the hamster, the most frequently appearing anomaly was poor ossification in the head region. There was no maternal mortality at the doses tested.

Robens (1969) studied the teratology of carbaryl, diazinon, norea, disulfiram, and thiram in guinea pigs, rabbits, and hamsters. Carbaryl was teratogenic only in the guinea pig. Diazinon and norea were without effect in the hamster, and thiram was teratogenic in the hamster, but not disulfiram. The doses of carbaryl and thiram used in this study were about 1000 times the allowable limit on crops. Smalley (1968) studied the teratogenic action of carbaryl in beagle dogs. He found terata at all levels tested but no dose response relationship was apparent.

Carbaryl was also reported in the Bionetics study as being teratogenic when used in DMSO vehicle. DMSO itself, however, produced abnormal fetuses. Courtney (1960b) found an increased incidence of microphthalmia. No teratology was produced when carbaryl was tested in an AKR strain of mouse.

Khera and Whitta (1968) found that paraquat induced high incidence of costal cartilage formation in rat embryos.

Robens (1970) also studied the teratogenic activity in the hamster of Captan, Folpet, Difoltan, Hercules 14503, and all thalidomide derivatives which have current or proposed uses as fungicides. Terata were produced depending upon the day of organogenesis on which these compounds were administered.

Kennedy et al. (1968) conversely found that Captan, Folpet, and Difoltan were not teratogenic in two strains of rabbits and in Charles River rats. Captan in hamsters produced no increase in terata above those of controls.

The Bionetics study found no significant increase in anomalies when Captan and Folpet were tested for teratogenicity in both AKR and C57 strains of mice.

Few reports of teratogenic studies with organophosphates have appeared. Rumsey (1969) immersed rats in solutions of Rulene during the gestation period; no teratogenic effects were noted. Klotzsche (1970) found no terata in rabbits with the organophosphate insecticides Ekatin® (thiometon) and Anthio® (formothion).

Khera and Clegg (1969) described the earlier literature of organophosphates with respect to teratogenic potential and indicated that the data are inconclusive.

Khera and Whitta (1968) found that one i.p. injection of paraquat on day 6 of gestation induced a high incidence of costal cartilage malformations in the fetuses. The defect was not noted when paraquat was given on days 7 through 14 of gestation.

There appears to be no real conclusive evidence that this small number of pesticides which have been studied for teratogenic potential actually represent a hazard to humans under normal conditions of pesticide exposure. It is difficult to extrapolate teratogenic findings from animals to man because of differences in sensitivity to the pesticide and frequently differences in metabolic pathways. However, it is apparent that much more research needs to be done in this area.

2. Mutagenesis

A number of chemicals now in our environment have been shown to be mutagenic to some form of cell. The science of mutagenesis is the study of mutations or any inherited change in the genetic material of an organism.

Although mutations can occur anywhere in an organism structure, cell biologists are particularly interested in gene mutations or chromosomal alterations that are transmitted by way of the sperm or the ovum to the next generation, since genetic damage has never been shown to be reversible. The lesions which can occur in the DNA of the chromosomes are few in number and can be recognized by methods presently in use.

Although no pesticide in wide use has been demonstrated to be mutagenic in all the presently available test systems, the great majority have not been thoroughly tested.

Interest in genetic damage was aroused after Muller in 1927 showed that high energy radiation (X-rays) caused mutations in fruit fly gametes, and that mutations occurred both in the genes and in the chromosomes. During World War II gene mutations and chromosome breaks were produced in fruit flies with chemical agents, particularly the nitrogen mustard group of compounds. In screening chemicals for possible mutagenicity, it is well to test for both gene mutations and chromosomes breaks. Some chemicals produce very few chromosome breaks, but induce immense numbers of gene mutations.

The methodology for mutagenicity testing of chemicals in the environment is in its infancy and there is no firm agreement among the investigators as to the kind or number of tests which are needed to prove that a chemical is or is not mutagenic (does or does not represent possible mutagenic hazard for man). The currently used procedures for testing mutagenic activity of drugs, pesticides, and other chemicals, fall into four categories:

(1) Sub-mammalian tests.

(a) Bacterial Systems (Whitfield _et al_., 1966).

(b) Neurospora (de Serres and Osterbind, 1962).

(c) Drosophila (Muller and Oster, 1963; Parker, 1954).

The problem of metabolism, detoxification and permeability of the test agent in these isolated sub-mammalian systems makes extrapolation to mammalian systems difficult.

(2) Cytogenicity of mammalian cell cultures (Puck and Kao, 1967). The mutagenic effect of mammalian cells can be measured both _in vivo_ and _in vitro_.

(3) The Host-mediated Assay (Gabridge and Legator, 1969).

(4) Mammalian tests.

(a) Specific Locus Test (Russell, 1951).

(b) Dominant Lethal Tests (Bateman, 1958).

Epstein (1970) advocates use of the dominant lethal test because "80% of gene mutations in man are attributable to dominant autosomal traits".

Literature dealing with mutagenicity of pesticides comprises more than 500 papers. Most of these tests were done in plants and the information on the mutagenic potential of widely used pesticides for mammalian systems is sparse. Captan was tested by Legator (1970) for mutagenicity in E. coli, L-132 embryonic lung cells and rat-kangaroo cells in tissue culture. The mutation rate in E. coli was increased at high concentrations and the number of chromosome breaks in both the L-132 lung cell culture and rat-kangaroo cell culture were increased. Epstein and Shafner (1968) screened a number of chemicals in the environment for possible mutagenicity as measured by the dominant lethal test in Swiss mice. The pesticides used included captan, DDT and maleic hydrazide, and all yielded a mutagenic index in the range of that given by control animals. TEPA and METEPA, which have been proposed for use as insect chemisterilants (LaBreque, 1961), have all been confirmed as having mutagenic potential (Epstein and Shafner, 1968). Preliminary studies by Legator (1970) indicate that the insecticide p,p'-DDT is capable of inducing dominant lethal mutations in rats. Palmer et al. (1970) studied the effects of DDT, DDD, DDE, and DDA on rat-kangaroo cells in culture. The p,p'-forms of DDT, DDD, and DDE produced twice as many chromsome breaks as did the corresponding o,p'-forms. Tsoneba-Maneva et al. (1969) produced chromosomal aberrations with the organophosphate diazinon in human lymphocytes in culture.

Mutagenicity is becoming increasingly important to humans. As life expectancy is lengthened through control of parasitic and bacterial diseases, morbidity from genetic weaknesses caused by mutation is increasing. Mutational effects may continue for many generations after the mutation has occurred.

An important area is the effects of exposure to combinations of compounds. The possibility of pesticides potentiating other pesticides or other chemical agents to become mutagens has not been explored.

In addition to the in vitro and in vivo cytogenic and the mammalian tests for mutagenesis, population monitoring should also be included in any overall program aimed at controlling mutations.

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PROTECTION OF WORKERS FROM PESTICIDE EXPOSURE

Homer R. Wolfe

Workers are often subjected to relatively high levels of pesticide compounds when actively engaged in pest control operations or working directly with the compounds in formulating or manufacturing plants. Illnesses resulting from overexposure to pesticide chemicals do occur among such workers. Most, however, are a result of carelessness or accident. Experience has shown that if proper precautionary measures and directions are followed even the more toxic compounds can be used safely.

Even though there is an effort to insure that all pesticides produced in the future will be low in toxicity to warm-blooded animals and not persistent in the environment, any great change in this direction will probably not take place in a very short period of time. Thus, at least in the immediate future, we can expect to see continued use of compounds that are relatively toxic to warm-blooded animals. In fact, several of the new compounds that have reached the point of registration during the last couple of years have acute oral LD_{50} values of less than 50, which indicates that they are highly toxic. Also, we have no firm assurance that less persistent compounds developed within the next few years as replacements for persistent pesticides now being used will be of low mammalian toxicity. Thus, we should not lessen our concern about the acute hazard to persons who come in contact with such compounds. Protection of such persons from exposure is necessary if a good record for safe use and handling of pesticides is to be maintained.

Much of the safety in relation to pesticides rests on the user or applicator of the compounds. If he is knowledgeable concerning pesticides and understands the importance of taking proper precautions he can do much to insure the safety of himself and others. This also applies to workers involved in the manufacture and formulation of toxic compounds. Their contact is usually with the more concentrated forms of pesticides; therefore, they should be especially aware of the need for protecting themselves from exposure. Thus, an important adjunct to safety in relation to pesticides is education, not only of supervisory personnel but also of those individuals who actually handle the materials.

There are several very important indirect ways of protecting the worker such as providing education and medical supervision, stressing the importance of personal hygiene and cleanliness, the importance of not being careless, and pointing out the need for reading and following directions on the pesticide label. However, these topics will be covered by other presentations on this program. The main purpose of this presentation is to discuss the more direct protection of the various routes of entry of pesticide into the body. Protection of these routes means prevention of exposure and prevention of exposure is undoubtedly the best insurance against poisoning.

ROUTES OF ENTRY

There are four routes of entry of pesticide compounds into the body: (1) dermal, (2) respiratory, (3) oral, and (4) through cuts or abrasions in the skin.

DERMAL ROUTE

The dermal route is considered to be the most important route of entry into the body during most exposure situations in the field and probably plays an important part in exposure of workers in formulating plants. This route is one that has undoubtedly been responsible for a great many poisonings of workers, especially from the more toxic organophosphorus compounds.

In research studies we have measured the potential exposure of several hundred pesticide applicators, and the results indicate that over 97% of the pesticide to which the body is subjected during most exposure situations, and especially to applicators of liquid sprays, is deposited on the skin. It should be understood that any given amount of pesticide is more rapidly and more completely absorbed by the oral or respiratory routes. However, absorption of pesticides by these two routes is probably too small a fraction of the total potential exposure to be considered the main factor in most poisoning cases of workers in the field.

In one set of experiments, for example, we have calculated the potential dermal exposure of orchard spraymen to parathion to be approximately 19 mg/hr; however, the potential respiratory exposure was calculated to be only 0.02 mg/hr of exposure.[6] This indicates that there is potentially 950 times more dermal exposure than respiratory exposure to workers in that type of application operation. Thus, if only a small fraction of the potential dermal exposure was to be completely absorbed it would probably still be more than the respiratory exposure. The respiratory route, however, takes on increased importance when exposure is to vapors, fine dusts, fogs, or aerosols made up of very small droplets.

The importance of protecting specific body areas has not been clearly defined in the past. This is because the rate of absorption of different compounds through human skin is difficult to measure with any degree of accuracy. The most useful and probably most accurate estimations or measurements on the percutaneous penetration of pesticides in man which have been accomplished thus far have been made by Maibach and Feldman.[1] Using radioactive labeled pesticides they were able to determine approximately what fraction of an applied dose would be absorbed through the skin. In this way they not only compared the degree of dermal absorption for certain pesticides but also compared absorption of a single pesticide for different parts of the human body. The results obtained indicate that sufficient importance may not have been attached to protection of certain body areas.

Lower Trunk and Legs.--In checking dermal penetration of parathion at different body areas these researchers found that the area of greatest absorption on man is the scrotum where approximately 100% of an applied dose was absorbed. The possibility of pesticide on this body area being completely absorbed is a very important point and emphasizes the need for increased concern about protection of the area. Of utmost importance would be the need for extreme caution in order to avoid spillage of highly toxic liquid pesticide onto the scrotum.

Although cloth coveralls or trousers provide a reasonable amount of protection where contamination does not easily penetrate clothing, the wearing of waterproof trousers provides the best protection for the lower trunk and leg areas and is especially recommended in work situations where there is chance of liquid spillage, soaking by continued contact with more dilute liquid sprays, or penetration of clothing through excessive contact with dry pesticides. In formulating plants where the main outer protective garment is usually cotton coveralls, workers should be required to wear waterproof aprons, especially if they are on duty at bagging or mixing stations where there is often considerable contamination down the front of the clothing with relatively concentrated wettable powder formulations. Fortunately, many plants require the use of aprons. Even when the waterproof apron is used it is very important that the worker change to freshly laundered clothing each day in order to prevent contamination of the scrotum or other skin areas. Needless to say, use of clean clothing and daily bathing in an effort to avoid excess dermal absorption are essential in any type of exposure situation.

Upper Trunk and Arms.--Protection of the upper trunk and arms from contamination by toxic pesticides is important, especially under conditions where heavy spray drift may thoroughly wet cloth shirts, coveralls, and underclothing or where concentrated dry pesticides come in contact with clothing and skin in formulating plants. Our studies have shown that the greatest potential contamination of spraymen in this general body area is the upper back, shoulders, and forearms of workers operating equipment which propels spray up into the air where it is more subject to drift. Under these conditions a waterproof jacket or raincoat provides the best protection for this general body area. This gear is usually worn during cooler conditions, but as the temperature rises and the clothing becomes unbearably hot to wear, workers tend to discard them and work with much less protection--perhaps only a short-sleeved T-shirt-type undershirt on the upper trunk area. Under such conditions workers should be encouraged to at least wear a long-sleeved cloth jacket that will not be easily penetrated by pesticide, and preferably one that can be properly washed.

The wearing of long-sleeved heavy grade "GI" cotton shirts or coveralls as outer clothing during hot weather, often with no underclothing, is popular with many applicators even though this is not a recommended practice. Fortunately, these items of outer clothing provide a reasonable amount of protection where spray drift is light with very fine droplets that do not wet through to the skin. Under such conditions the clothing should be changed and laundered daily. If clothing used during spraying such as shirts, jackets, or coveralls are merely hung up to dry after work and used repeatedly, as is often the practice, it doesn't take long for the pesticide material to work through where it will make contact with underclothes or skin.

In selecting protective clothing for workers it is important to take into consideration the comfort of the individual when he wears such items. The conventional black or dark green rubberized or plastic waterproof jackets in common use during past years are considered by many applicators to be uncomfortable to wear not only because of greater heat absorption but also because they may be of heavy grade material and not very flexible.

During recent years, however, several jackets and jacket-trouser combinations that are lighter in color and weight have been available. Although less durable, they are less costly to replace. Our tests have shown that a light yellow or white waterproof jacket may reflect enough heat to cause the temperature at the skin surface to be as much as 8 to 10°F lower than when wearing a black jacket under certain conditions of intense sunlight when ambient temperature is approximately 90°F. Nevertheless, there is still considerable discomfort in wearing any waterproof clothing during hot weather because of the trapping of body heat.

Disposable paper jackets have been tested and found suitable for use only under conditions where heavy wetting does not occur. Such paper jackets were found to be much cooler and thus more comfortable than other jackets tested.

Observations of pesticide applicators have indicated that although waterproof clothing items, and especially jackets, are usually carried by the workers, or readily available to him, he usually will not don the clothing until drift of pesticide increases to the point where he feels protection is necessary. Unfortunately, by this time there is often considerable contamination of skin and clothing. The covering of contaminated skin areas by waterproof clothing may create conditions under which dermal absorption may be increased. This may be more important during hot weather where high temperatures and perspiration are involved. Whether or not there would be less absorption under these conditions than if the clothing were left off entirely depends upon the potential exposure which might occur after the worker puts on the clothing. Maibach and Feldman[1] found that covering up (occlusion) of contaminated skin with thin plastic wrap material caused approximately a four-fold increase in absorption of parathion. Although the increase of absorption of pesticide by covering contaminated skin with various items of protective clothing is not known, the above occlusion test results are cause to emphasize the need to put on protective gear before the skin has been contaminated to any great degree.

The use of waterproof jackets in pesticide formulating plants is not common and generally not considered a requirement if, as stated earlier, rubber aprons are worn and coveralls are kept clean. It should be noted, however, that in a plant there is easier immediate access to showers and other means of decontamination, should excess exposure occur, than in the field where applicators work.

Head-Neck Area.--Results of the dermal absorption studies noted above indicate that the head-neck area should be given more attention. In this area absorption of parathion was found to be from 32 to 47% of an applied dose;[1] much more than we would have anticipated and more than at other areas of the body studied with the exception of the armpit and scrotum. When observing either pesticide applicators or workers in formulating plants it is easy to conclude that the face-neck area is less protected than most other parts of the body. Head coverings or caps used in formulating plants are often made of material that allows easy penetration of pesticide onto the scalp. The headgear may have no bill or brim which would provide some added protection to the face-neck area, especially from pesticide material which drifts downward.

Protection from downward drift is especially important during application of liquid sprays. The headgear most commonly used by pesticide applicators is the billed cap which provides some protection for the face but very little for the remainder of the head-neck area other than the scalp. The conventional "Sou'wester" rain hat, often used when heavy downward drift occurs, does not provide exceptionally good protection for the face and sides of the neck. This is because of the narrow brim in all areas except at the back of the neck. Metal or fiber "hard hats" are also used to some extent; however, most have too narrow a brim to provide adequate protection. "Hard hats" which allow circulation of air over the head under the hat should not be used where exposure is to toxic dusts.

Our studies have shown that the greatest protection from downward drift of pesticides is afforded by some type of wide-brimmed hat, preferably made of water-repellent material. Waterproof hats, other than the "Sou'wester," were not readily available at that time. However, one is now available which is waterproof and also has a wide brim that affords good protection of the face-neck area. This type of hat should be recommended for use by all applicators who may be subjected to downward drift of pesticides.

Of particular interest in relation to exposure of the head-neck area is the finding by Maibach and Feldman[1] that absorption of parathion is relatively efficient (47% of applied dose) in the ear canal. Exposure in this area could occur through drift of fine pesticide mists or dusts or by digging in the ear with the tip of a contaminated finger. Of particular importance is the potential for drift into the ear of concentrated dry formulations of toxic compounds in the formulating plant.

It is of importance to note that wearing goggles and respirators provides considerable protection to the face.

Although a statement suggesting the use of goggles can be found on certain pesticide labels, they are rarely worn except by pilots who apply pesticides by aircraft. Questioning of pilots has revealed that they wear goggles not only to prevent poisoning and to keep wind out of the eyes but also to prevent certain organophosphorus pesticides that are direct inhibitors of cholinesterase from causing miosis. This is understandable because it has been shown that unilateral contamination of the eye with TEPP may cause pilots to inadequately judge distance.[4] The incoordination which may accompany this could be a serious threat to safety.

Hands.--The hands are often the body area having the highest exposure to pesticides and they have a greater chance of coming in contact with the more concentrate formulations. They are also more subject to cuts or abrasions, which will be discussed later.

High potential exposure to the hands brings attention to the need for wearing gloves. Some people who have worked with pesticides feel it is better not to wear gloves than to wear gloves that are contaminated on the inside; something which invariably occurs to some degree. Our research concerning the use of protective gloves indicates that, unless there is gross contamination of the inside of the gloves, the potential exposure is less when wearing gloves than when not wearing them. If gloves are kept clean on the inside there is very little doubt concerning the value of their use when handling pesticides. Unlined rubber gauntlet gloves provide the best protection because the gauntlet covers the wrist area not normally covered by the jacket sleeve and they can be turned wrong side out for proper cleansing of the unlined inside surface.

Feet.--Waterproof shoes or boots should be worn when handling or applying pesticides on a large scale. During liquid spray operations the ground cover of weeds, grasses, or other plants invariably becomes wet with dilute pesticide regardless of whether or not it is the target of the application. Shoes quickly become contaminated when walking through such plant growth. When leather shoes become wet with spray material they have a tendency to become cracked and dried out to the extent that pesticide easily penetrates through to the sock or foot. Both leather and canvas shoes absorb chemicals and may hold them in contact with the wearer. Boots should be washed and dried thoroughly, inside and out, as frequently as needed to remove any pesticide contaminant.

Workers in pesticide formulating plants should wear waterproof boots. Coverall pant legs should be worn outside the boot tops to prevent sifting of dry concentrated pesticide into the footwear.

RESPIRATORY ROUTE

Protection of the respiratory route is especially important where toxic dusts and vapors or very small spray droplets are prevalent, or where application is in confined spaces. Extremely fine particles and droplets found in dusts and mists are much more easily drawn into the respiratory system than the larger droplets formed by most conventional dilute spray machines. Our tests have shown that when operating an 8X (eight times the normal dilute concentration) concentrate airblast machine in fruit orchards the potential respiratory exposure is nearly 3 times greater than when operating the conventional dilute machine.[6]

Respiratory protection for most types of application can be provided by use of cartridge-type respirators or, in certain cases, gas masks with special cannisters which have greater adsorbent capacity than the cartridges. Applicator pilots who risk the possibility of flying through drift of fine droplets or dusts should use a face mask equipped with a filter cannister and attached either to their belt or to the inside of the cockpit. When fumigating or applying highly toxic pesticides in confined spaces it is advisable to use a respirator with a special compressed air supply tank so that none of the contaminated ambient air is inhaled.

Proper care of respirators is very important to the protection of the workers. The rubber face-piece becomes hardened and the head straps lose their elasticity with age and exposure to heat and sunlight. These conditions lead to poor fit and allow leakage around the face-piece. Two of the more common offenses in the care of respirators that we have observed are (1) failing to occasionally wash the face-piece with soap and water and (2) neglecting to change the filter cartridges or cannisters regularly. Washing of the face-piece of a cartridge-type respirator should not be attempted while the cartridges are in place as moisture may contact the activated charcoal filter material and reduce its effectiveness in adsorption and absorption of pesticides. Solvents should not be used as a cleaner for they may damage certain parts of the respirator. The general recommendation is that cartridges should be changed after 8 hours of continuous exposure. In most application situations this leaves much up to the individual worker to keep a record of his respirator exposure time. In a formulating plant where hours of exposure are more regular this is more easily controlled under the guidance of a foreman. Under conditions of intense exposure the useful life of the cartridge is much shorter. Thus, if the breathing seems hampered, or if the odor of pesticide is detected, the filter cartridges should be changed immediately. If the outer filter pads are separate removable units they should be changed more frequently than the cartridges.

During discussions of the respiratory route of entry into the body the question is often raised concerning the hazard of smoking pesticide-contaminated cigarettes. We have found it difficult to measure such potential exposure with any great degree of accuracy. The technique we have utilized thus far involves subjecting the cigarettes to normal handling through the process of removing them from the pack and placing them in the mouth, lighting them, and smoking one-half the cigarette. The remainder of the cigarette is then analyzed for pesticide content. The values obtained are based on the assumption that pesticide on the cigarette will be volatilized before being broken down by burning and that none of the volatile or particulate pesticide would be trapped in the butt end of the cigarette. In observing smoking by workers it was noted that the area of greatest contamination of the cigarette was far enough from the butt end to allow burning of the contaminated area in most cases.

In studies of cigarette contamination by spraymen applying endrin in orchards, the potential exposure through smoking during application operations was calculated to be not more than 0.002 mg per cigarette, even when the cigarettes were handled with hands wet with the dilute spray.[8] In later studies[7] involving spraymen applying parathion to apple orchards by airblast machines, from 0.003 to 0.005 mg of parathion per cigarette could be recovered where they were handled with hands that were contaminated but dry. When handled with hands that were wet enough with dilute spray to leave moist spots on the cigarette paper from 0.020 to 0.050 mg could be found. In a controlled study designed to determine what might be the maximum contamination of cigarettes through such handling, hands were dipped in 45% emulsifiable concentrate parathion, the hands wiped off lightly on the trousers, and the cigarettes were handled to simulate smoking. The highest value found was 0.235 mg per cigarette.

Even though values for potential respiratory exposure through smoking contaminated cigarettes may not appear to reflect any great hazard, two important points must be kept in mind: (1) Pesticide entering by the respiratory route is practically 100% absorbed, and (2) There is no assurance that a more toxic breakdown product will not be formed and inhaled as the high temperature of a burning cigarette reaches the contaminated areas rather than complete destruction of the compound by burning. For example, in the case of parathion the oxidation product, paraoxon, is estimated to be much more toxic than the parent compound, possibly 100 to 500 times more toxic. This could be an important factor as far as hazard is concerned and emphasizes the need for recommending washing of hands and face before smoking.

ORAL ROUTE

There has been little experimental work conducted to define the magnitude of oral exposure. We are studying techniques at the present time. Analysis of saliva samples of exposed individuals appears to give some indication of contamination.

The most serious oral exposure may be brought about by splashing of liquid concentrate into the mouth while pouring and measuring pesticides. Contamination may also occur through licking the lips, by rubbing the mouth with contaminated arms or hands, by careless actions such as attempting to blow out clogged spray nozzles with the mouth, or by eating or drinking with contaminated hands.

We have attempted to measure the parathion contamination of typical sack lunch items, such as sandwiches, cookies, and pickles by workers whose hands had been contaminated while thinning fruit in recently sprayed apple orchards.[5] A lunch consisting of four half-sandwiches, two cookies, and one pickle was given to workers who handled and ate one-half of each item with unwashed hands. The other half of each item was analyzed for parathion. This provided potential oral exposure values for lunch items. A total of approximately 0.103 mg of parathion was found on the typical lunch mentioned above. Although this is not a great amount of pesticide, it would add to the total exposure of each individual; thus, workers should wash hands and face before eating.

ENTRY THROUGH CUTS OR ABRASIONS

Any break in the skin may allow a more direct route of entry into the blood stream. Even if the outer layer of dead cells (strateum corneum) of the skin is removed by scratching or scuffing the result may be a potential for increased absorption at that site as this layer of cells is considered the main barrier against chemicals. Maibach and Feldman[1] found that when most of these cells were removed by abrading through repeated application and removal of sticky tape, the absorption of parathion applied to the forearm could be increased more than 8-fold.

This route of entry is one that may not have received enough attention in the past. Cuts and abrasions occur most frequently on the hands, and unfortunately the hands are the body area most often in contact with the more concentrate forms of pesticides. There have been poisoning cases suspected as having been a result of entry by this route; however, there has not been enough evidence to definitely prove that this route played the major part in the illnesses.

One suspected poisoning case which might be used as an example involved a 25-year-old worker in a pesticide plant whose finger was crushed by a fork lift which appeared to be contaminated with concentrate parathion.[2] For several weeks prior to the accident he had been working primarily with carbaryl, along with a small amount of malathion, but nothing as toxic as parathion. The worker became severely ill and exhibited symptoms of poisoning within approximately 30 minutes of the accident, a coincidence which aroused suspicion that the illness was associated with the accident. Analysis of a blood sample showed cholinesterase activity to be very low. There was prompt clinical response to administration of atropine and 2-PAM. Although there does not appear to be enough evidence to prove entry of pesticide at the area of broken skin, the circumstances around the case indicate that this route of entry could possibly have played a major part in poisoning. In such case poisoning symptoms may not have developed had the worker been wearing gloves.

Another suspected case involved broken skin on the feet of a 54-year-old male who wore canvas shoes while spraying an apple orchard.[3] His shoes became soaked with the dilute spray from walking through wet cover crop. He had complained of "scalded feet" indicating raw, red, oozing areas especially on his soles and between his toes. On several occasions he was aided in bandaging his feet or procuring tape, etc. by co-workers. He had sprayed for several days but on the day of his death he had sprayed for 9 hours, wearing canvas shoes all day. A post-mortem blood sample showed very low cholinesterase. The physician investigating the case indicated that cause of death was parathion poisoning due to probable dermal absorption particularly through an area of dermatitis on both feet. Because body areas other than the feet were exposed there is no complete assurance that this was the main route of entry of the compound. Nevertheless, this case points out the importance of wearing rubber boots or shoes while applying liquid pesticides.

DISCUSSION

Regardless of how specifically the measures for protection of workers from exposure to toxic pesticides may be stated for any particular situation, people who work with such compounds must realize that there is some element of risk involved. Accidents occur, even among workers who are careful. In case of accidental gross contamination of skin with a highly toxic compound every effort must be made to cleanse the contaminated area as quickly and as thoroughly as possible. The best recommendation at present is the use of plenty of soap and water. Wash by rubbing with the hands or with a piece of cloth. Do not scrub with a brush because the outer protective layer of the skin may be abraded enough to allow more rapid absorption of any pesticide not removed. A bar of soap, towel, and container of water should be carried on every pesticide application machine or accompanying vehicle for use in washing should a spillage occur. In the pesticide formulating plant shower facilities for use in case of accidental contamination are practically always near at hand. If pesticide gets in the eyes they should be thoroughly flushed with water for at least five minutes. If a person should feel ill while working with pesticides he should stop work at once and get medical attention. If his illness is diagnosed as being caused by a pesticide he should not return to work until a physician advises that it is safe to do so.

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APPLICATION OF SOLID WASTES RESEARCH TO PESTICIDE DISPOSAL

H. Johnson[1] and A. W. Breidenbach[2]

The Solid Wastes Office (SWO) performs research, in-house or through grants and contracts, to develop new and improved methods for handling and disposing of all solid wastes with the exception of those wastes associated with the mineral and fossil fuel industries which are handled by the Department of Interior. Therefore, in the past, studies bearing on disposal of pesticide containers, and the effects of pesticides on various solid wastes processes, namely incineration, composting and landfilling, were clearly within the responsibility of the SWO.

The number of projects directly pointed to pesticide disposal being sponsored by the SWO is relatively small. However, there are quite a number of projects designed to improve overall solid waste handling and disposal operations and they hold great potential in their application to special wastes such as pesticides. I will therefore present the SWO's pesticide disposal program as projects not directly pesticide oriented and secondly as those projects which are directly pointed to or involving pesticide disposal. In both cases, the avoidance of environmental pollution is the basic consideration.

Incineration is a solid waste volume reduction technique which has received fairly wide application, both by municipalities and in certain institutional situations, such as hospitals. The incineration of special wastes poses potential health hazards from the standpoint of air pollution and the quality of ash and residue which must ultimately be deposited on the land, perferably in a sanitary landfill. The Bureau of Solid Waste Management has sponsored research at Harvard University for evaluating the feasibility of incinerating low-level radioactive wastes, with particular attention to the distribution of isotopes between flue gases, residue, furnace linings and duct surfaces for various types of incinerators. The mechanized steam boiler appeared to be most satisfactory, and the results of this study might well have application for incineration of wastes with high levels of pesticide residue, such as pesticide containers.

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Perhaps one of the most advanced concepts in incineration - and in solid waste management systems - is the CPU-400, which is being developed under contract by the Combustion Power Company of Palo Alto, California. Basically, the CPU-400 is planned as a fluidized bed incinerator which will burn refuse at high pressure, producing hot gases to power a turbine which will in turn drive an electrical generator. Municipal solid wastes constitute a better fuel than generally imagined - having a heating value of 5,000 Btu per pound, or approximately 1/3 that of a good grade of coal. As designed, the CPU-400 should produce approximately 15,000 Kilowatts of electricity, while reducing 400 tons of municipal refuse daily; the generator units are expected to supply between 5 to 10 percent of the electric power requirements of the community providing the refuse, thus offsetting part of the cost of waste disposal.

In addition to power generation, up to 3/4 of the heat in the gas turbine cycle would be available for such auxiliary functions as steam production, drying sewage sludge, or saline water conversion. Developmental work on the CPU-400 also contemplates use of the immense vacuum produced by the gas turbine to convey refuse to the incinerator from individual dwellings or collection points in the city through underground pipes. Such pneumatic collection systems are already being successfully employed in Sweden and Great Britain.

One of the essential attributes which the CPU-400 must display in order to be practical, is the ability to receive, and safely handle virtually all types of solid wastes. And this would, of course, include wastes containing pesticide residues. So far, we are encouraged to believe that the CPU-400 will be able to incinerate substantially every type of solid waste without environmental hazard.

The sanitary landfill is regarded by the Bureau of Solid Waste Management as the most important land disposal method, and consequently a considerable research and development effort is directed toward improving this technique and assuring its safety from the pollution standpoint. If properly located and engineered, one of the most favorable qualities of the sanitary landfill is its ability to receive a heterogeneous solid waste load which varies from being relatively innocuous and chemically inert plastics and aluminum, to being putrescible and even toxic materials.

For every sanitary landfill, and particulary those receiving such toxic materials as pesticide residues, it is important to assure that there is no contamination of nearby ground and surface waters. A Bureau sponsored study is being performed by researchers at the University of Illinois, on the hydrology of several-solid waste disposal sites. Data from the study is useful in evaluating the factors that control groundwater and landfill leachate movement. Five different hydrogeologic environments were selected for the study and piezometers were installed in drill holes, stragetically located to define fluid potential distribution, and water samples were taken for chemical analysis. In addition to total dissolved solids and chlorides, which are good indicators of leaching, a host of chemical determinations were done on those samples. The results were used to predict the best physical placement of landfills to avoid leaching. No pesticides were detected in the leachate during the time of the study.

Oceanic disposal of solid wastes, including pesticides and other toxic materials, may be an alternate to the sanitary landfill method; however, there are many questions to be answered before the Solid Wastes Office could endorse ocean disposal. A contract has been let to the Applied Oceanography Branch of the Dillingham Corporation, San Diego, California, for the purpose of determining the nature and magnitude of present ocean disposal practices. The Dillingham study was also to determine what present or potential effects know ocean disposal activities may have on public health or community esthetics. In connection with the study, on-site surveys were conducted at 16 U.S. cities situated on or near the Atlantic and Pacific coasts, and the Gulf of Mexico.

Preliminary estimates from the study reveal that some 48 million tons of waste are being disposed of at sea each year at a cost of $29 million, inclusive of dredging spoils but excluding outdated munitions. Methods employed for disposal consist primarily of transporting the wastes in bulk or barrels aboard self propelled or towed barges. The majority of wastes are disposed of in bulk form and discharged while underway.

In several cases, highly toxic chemical wastes have been carried to sea aboard merchant ships as deck cargo. The containers were then discharged in undetermined areas once the ship was 300 miles from land. However, bulk industrial wastes are usually transported in tank barges certified for ocean waters by the U.S. Coast Guard. In addition, U. S. Coast Guard regulations regarding the bulk shipment of chemicals by water must be adhered to. The Sparkling Waters is just such a barge especially built to handle insecticides and other toxic chemical wastes off the New York coast.

A bridge between projects pointed to improve the overall Solid Waste Management program and projects directed specifically to pesticide disposal can be seen in the concept or recycling and reuse of waste material. Some of the present barriers to increased utilization are technological and others are economic. Overcoming these barriers is an important goal of the Bureau because success in increasing the amount of waste that can be reused has the dual advantage of reducing the amount which must be disposed while conserving the nation's natural resources.

Cellulosic wastes, including wood, bark, sawdust, oat hulls, corn cobs, bagasse and other agricultural residues are generated in truly prodigious quantities. Little, if any significant portion of these wastes is beneficially used and, since they are commonly burned, cellulosic wastes often contribute to air pollution in areas where they accumulate. Under a reresearch grant, the Institute of Forest Products, University of Washington, in Seattle, is developing a unique means for utilizing cellulosic wastes which will at the same time allow safer and more efficient application of pesticides to the soil.

Some common properties of the wood and agricultural wastes are that they consist predominantly of polymeric cellulose macromolecules; they contain an abundance of replaceable hydrogen atoms; and all are biodegradable. Since these waste materials are polymers containing replaceable hydrogen atoms it should be possible to attach pesticides to these substrates in the same way that acetic acid, for example, becomes attached to cellulose in the manufacture of cellulose acetate. Research has shown that pesticides can be attached to such solid waste as sawdust, bark, and lignin by means of ester linkages. Herbicides have been combined with natural as well as synthetic polymers. The herbicides used were 2, 4-D, 2, 4, 5-T, 4(2, 4, 5)-TB, and Dalapon. It was found that each of these polymeric combinations prevented the germination of certain seeds longer than the herbicide alone under controlled laboratory conditions. Future plans are to test these polymers under field conditions.

The practical implications for the ability to chemically bond pesticides to cellulosic materials, is that very large quantities of cellulosic wastes, so treated, could be utilized as a mulch for gardens and in agriculture. The pesticide in the mulch would be released in controlled fashion with distinct advantages over present procedures for applying pesticides to soils. Now, pesticides usually have rather short useful lives because they may be degraded by bacteria to inactive metabolites, or washed by rainwater into the subsoil where they are inaccessible to pests they are intended to control. Also, and more important from the public health standpoint, this leaching into the subsoil often means that some rather stable pesticides, or their degradation products, find their way into potable water supplies.

In contrast, if the pesticide were chemically combined with the polymeric solid waste, its useful life should be prolonged; attack by bacteria should be reduced; and the pesticide should not be leachable into the subsoil and hence will not pollute streams and rivers. As the solid waste-pesticide mulch lies on and in the soil it will gradually decompose, continually releasing the active pesticide over a long period of time. With this technique the problems and potential errors of measuring and diluting liquid concentrates are eliminated. Spillages of solid are, of course, less likely than liquid leakages and are easier to rectify when they occur. Controlled releases of the pesticides may also allow lower dosage and fewer applications.

Another very important implication for this project is the prospect it may hold for development and use of extremely short-lived biodegradable pesticides which, in combination with solid waste polymeric substrates, would be sufficiently stable for practical use. For example, many organophosphorous pesticides, are liquid and are too dermally toxic to permit their use by anyone other than virtually experts. Combinations of these materials would perhaps render them safe, while not destroying their biological activity. The currently "unuseable" pesticides are often effective at much lower dosages than the superficially less hazardous products that are now used in relatively massive amounts.

Composting of municipal and agricultural refuse is not widely used as a means for solid waste disposal in the United States. However, there are several compost plants in operation and one may reasonably expect to see the continued composting of solid waste on limited scale, in areas where the product is marketable. A research grant to the Western Research Laboratory of the National Canners Association, Berkeley, California, is supporting a study of the fate of insecticides in composted agricultural wastes. A substantial part of the fruits and vegetables received for preservation by canning or freezing is discarded as solid wastes. That portion of the raw product which is discarded - vegetable skin and rind - generally has the highest level of insecticide residue, and this fact has limited the use of such material as animal feed, and it also raises questions about possible harmful effects of spreading composted cannery wastes on agricultural lands. This concern is especially justified if toxic degradation or transformation products remain in the compost mixture.

The Canners Association study aims to obtain a better understanding of the mechanism by which insecticides are degraded by microbial or chemical action during aerobic composting, and also to obtain information which will make it possible to dispose of waste materials containing concentrated insecticide residues, without hazard to public health. Insecticides selected for the study represent examples of the three principal classes: Chlorinated hydrocarbons, organophosphates, and carbamates. The selection of specific insecticides was based upon the extent of usage in agricultural products, variety of chemical structure, and availability of reliable analytical methods. These included: dieldrin; parathion; diazinon; P, P'DDT; p - chlorophenyl, and with further studies planned for sevin and zineb.

While the study is still incomplete the break-down products of several insecticides have been identified and the varying effects of batch-type and Theromophilic composting processes have been noted. The summary in a recent progress report contained the following information:

1. Concentration of diazinon and parathion rapidly declined in both composting processes with the thermophilic process being the more efficient. Breakdown products identified for diazinon were oxodiazinon and sulphotepp. Those identified for parathion were aminoparathion, para aminophenol and paranitrophenol.

2. Continuous thermophilic composting caused some reduction in DDT whereas the batch process had little effect. No breakdown products have been identified.

3. Dieldrin was more efficiently degraded in the batch process and none of its breakdown products have been identified.

4. Following the active compost period (120 days), the curing or aging phase (180 days) of the process had little or no effect on the insecticide.

Recently, the SWO awarded a research grant to the Environmental Health Sciences Center at Oregon State University for purpose of studying the products of two waste sources, namely (1) the by-products of pesticide manufacturing and formulating industries and (2) the accumulations of containers generated by agricultural usage of pesticides. This entails decontamination and re-use of the containers and degradation of its unused residual content.

Using 2, 4-D and 2,4,5-T as their prime objectives, they will study the feasibility of transporting industrial waste liquor and by products of these two herbidices to an arid area in Oregon where they will be diluted and spread on the land for natural degradation. The 55 gallon drums will be chemically cleaned, compressed and buried or baled and reused as scrap metal. The theory behind the project is that herbicides and pesticides do not have an indefinite life in the environment. In every instance where persistance of pesticides in soil has been studied, it has been found that the chemical disappears with time to a level of little biological significance. The factors causing the disappearance are photochemical decomposition, chemical decomposition, microbiological degradation and physical factors such as adsorption volatilization or leaching.

Recently, a final report was received from a contract at Foster D. Snell Inc. in Florham Park, New Jersey on conditions necessary for decontamination and combustion of organic pesticides and pesticide containers. Work on this project has included:

1. Determining the temperature and rate at which pesticides burn in their pure form while testing the combustion gases for CO, CO_2, H_2O and intermediate organics.

2. Incorporating the same pesticides in a mass of material such as sawdust, paper, burlap, cloth, polyethylene and wood and investigating the burning temperature and rate and determining the combustion products.

3. Low cost chemicals including nitrates and chlorates were incorporated.in the pesticide and the pesticide-material mixtures above to facilitate decomposition.

The report received from this project indicated the structural and compositional requirements necessary for combustible pesticide containers and the possible use of polyethylene liners to aid combustion. It was shown during the course of the project that representative pesticides were virtually volatilized or sublimed when incinerated unless a binder was present to increase the residence time in the flame. By using polyethlene, which under heating or combustion conditions, softens or degrades to products of lower molecular weight, the advantages of a liner and a binder were obtained with one material and the pesticides studied could be essentially destroyed at temperatures normally acheived by burning wood, paper, cardboard, etc.

In conclusion, I hope my remarks today will give you some idea of the variety of projects sponsored by the Bureau of Solid Waste Management which have some direct or indirect bearing on the control of pesticide pollution in the environment. The results of many of our research projects are published in order that suggested benefits can be widely applied. We will certainly be pleased to make the results of projects cited, and results from other pertinent studies, available.

CONDUCTING FIELD INVESTIGATIONS OF SUSPECTED PESTICIDE INCIDENTS

Moses L. Anderson[1], Lynwood A. Fiedler[2], and Wilton Williams[3]

The principles of basic epidemiology, that are applied in the investigation of any disease or trauma affecting a certain population, are also used when pesticides are suspect. An epidemiological investigation should determine who was involved (the host), the responsible agent (pesticide), and the environmental situation which contributed to the occurrence of the incident. Once these factors are known it is possible to predict future occurrences and to take steps to prevent them from happening again. These methods have been used effectively by public health agencies in the control of communicable diseases, food-borne outbreaks, chronic disease, and others.

All pesticides are toxic chemicals, capable of producing illness and even death when misused. The extent of the morbidity or mortality will depend on many factors including the toxicity of the pesticide, route of exposure (oral, dermal, respiratory), the susceptibility of the person (s) or animal (s) involved, and others. Individual reactions will also vary depending on environmental factors (temperature, humidity, diet) and intrinsic factors (age, race, sex, physiological activity, subclinical pathology, fatigue, etc.).

Despite all the variables, trends are apparent in most poisoning investigations. The time interval between exposure and the onset of symptoms (incubation period) is generally short. Most acute exposures will produce symptoms within a few minutes. Concentrated solutions will produce symptoms earlier than a diluted one and an oral exposure will generally produce earlier symptoms than a dermal one.

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The United States has had very few mortalities due to contamination of food and clothing. Other countries have not been as fortunate, however, as their transportation and storage requirements are not as strict. Occupational exposure of agricultural workers has resulted in several incidents, however, which have caused tragedy, and will be described below.

Investigating cases such as these, requires cooperation between many agencies, people, and laboratory personnel. In one investigation in Arkansas the pollution control commission, extension service, mosquito control district, Fish and Wildlife Service, a medical center and others all worked together. More important perhaps than any other aspect is cooperation with a competent laboratory. Without an adequate sampling of specimens and a reliable analysis, very little can be gained from most investigations. For example, plastic containers should not be used since they will interfere with the analysis of some organochlorines. For this reason we have enclosed the paper "Sampling Procedures for Chemicals in the Environment" by William Barthel.

It is most helpful to use special forms for recording information while in the field. These forms act as a guide and help prevent the investigator from forgetting to gather essential data. We have enclosed one such form in use for investigating acute exposures.

NORTH CAROLINA PESTICIDE INVESTIGATIONS, 1970

Poisoning by chemical pesticides occurs at an undetermined rate in our society. Recently much attention has been devoted to pesticides and their adverse effects on man and his environment. North Carolina is one of 14 states in which State Services pesticide projects are sponsored by the national program here in Atlanta. One of the work units of these projects is to establish pesticide morbidity-mortality reporting systems whereby the extent of acute illness due to pesticides may be determined.

Such a system became effective in North Carolina in June, 1970. To set up the system, first a case report form was developed. This card was then distributed to the seven poison control centers in North Carolina and subsequently to all the state's physicians. Distribution to physicians was via the Epidemiological News and Communicable Disease Morbidity Report, a monthly publication in which timely pesticide notes are carried. Through this voluntary reporting system, all types of pesticide-induced illnesses are reported, including accidental ingestions by children, suicide attempts, and cases associated with formulation and agricultural use.

The response was almost immediate and we received reports of 80 pesticide cases with onsets from June 1 through September 30, 1970. Forty-seven of these cases involved organophosphorous insecticides.

As reports began to come in, we saw an increasing number associated with the spraying and harvesting of tobacco, North Carolina's leading agricultural crop. Of the forty-seven reported organophosphate cases, thirty-one cases indicated the insecticide parathion as causative. Twenty-five of these cases were investigated by the Division of Epidemiology. Two of the cases were found not to involve parathion and twenty-three were attributed to parathion poisoning at the conclusion of the investigations.

Our investigations were carried out by two physicians, two veterinarians, and a biologist, all members of the Division of Epidemiology in which the Pesticides Program operates.

The initial lead into a pesticide case usually was the case report card or a phone call from a physician or local health department. Occasionally an additional case was discovered while investigating a reported case.

The first step we made in pesticide poisoning investigations was to contact the attending physician to obtain his impressions and available medical reports. Then we proceeded with field investigations in which the victim, or his family and associates, were interviewed to ascertain the circumstances of exposure. We often called upon county health department sanitarians and public health nurses to assist in locating people involved.

In these cases we wanted to identify the product and the concentration of the active ingredient. We usually obtained this information from the pesticide container or from the person who bought it. We then wanted to know the exposure the victim had to the pesticide, his symptoms of poisoning, and when they occurred following exposure. The activities of the individual prior to onset were reviewed to see what other factors could be involved in his case. Following the investigation, a field report was written up on each case with hospital and medical records attached where applicable.

Of the twenty-five parathion cases we investigated in North Carolina, three were fatal and several others were hospitalized. Certain laboratory analyses are extremely important in positively diagnosing parathion poisoning. These are paranitrophenol detection in urinalysis and reduced plasma and red blood cholinesterase. Unfortunately, such analyses were not performed on most of the cases we investigated. However, based upon poisoning symptoms and response to atropine and 2-pam in these cases, we believe parathion was the responsible agent.

The following account of a specific case investigation should serve well to demonstrate what one may anticipate in such investigations:

On August 4, 1970, we received a telephone call from a physician who wished to report a pesticide poisoning case. He said the case had occurred in mid-July and that the victim, a 14-year-old farm boy, had experienced an extremely close call to death and that he was concerned that poisoning might again occur in this boy's family due to the lack of serious concern expressed by them during the incident.

An appointment was made with the reporting physician. By meeting with him, we obtained medical records on the case indicating that:

H. L. M., 14-year-old white male, was admitted to the hospital emergency room at 6:10 p. m. July 14, 1970, arrival being by ambulance from a neighboring county. He had been engaged in spraying tobacco with parathion that day and several days before, as stated by his parents. He had been apparently well until 3:10 p. m., July 14, 1970, when he began to complain of not feeling well. Shortly afterwards, he was noted by his mother to be quite weak and unable to use his arms and legs.

His symptoms at admission were nausea, vomiting, abdominal pain, respiratory distress, muscle fasiculations, absence of abdominal reflexes and hyperactive deep tendon reflexes.

Diagnosis was parathion intoxication and the patient was given IV (interveneous) atropine and protopam. He responded to treatment and was released from the hospital two days later on July 16, 1970.

The next step in the investigation was to interview the victim and his family. The investigating team consisted of a physician, a veterinarian, and a biologist. The first problem was locating the family, who lived in a rural county some 30 miles from the hospital where the case was treated. Using the names and address given to us by the physician, we obtained directions to the farm from the local post office. When we arrived at the farm, no one was home. The homestead was a typical one for this section. In the yard were dogs, a cat, chickens, and some swine running loose. The water supply was a dug well. Behind the house was a storage building with a padlock on the door. Between that building and the well was a pile of miscellaneous items, among them two badly weathered cardboard containers containing eight one-gallon glass jugs filled with a dark liquid. We examined one of the labels. Forty-six per cent ethyl parathion!

After inquiring at a neighbor's house, we learned the family was harvesting tobacco on another farm several miles away. We went there. When we arrived, we found the family and other workers "barning" tobacco in a tobacco curing barn. We introduced ourselves and explained that we were seeking information on the events leading to the boy's poisoning. The father and mother of the victim told us that the boy was spraying the diluted 46% parathion from a tractor with rear attached spray rig prior to his illness. He had sprayed for two days with no protective clothing and had not even worn a shirt. Then he "got sick" and they had to take him to the hospital. The day of the interview the boy was driving a tractor hauling tobacco from the field to the barn. He had recovered completely it seemed with no trouble since returning from the hospital. The family had eight other children, none of whom had been ill. The father tended to be completely unconcerned over the poisoning incident and was much more interested in demonstrating to us his new $2500 tobacco looping machine. Beside the barn lay an "empty" container of the 46% parathion with several teaspoons of the liquid still present.

This case points out the hazards of improper use of pesticides nicely. Beyond the fact that an acute poisoning case did occur, the potential was tremendous. Such investigations uncover these hazards and are used to lend support for stricter control of and better educational efforts in the use of pesticides.

Other pesticide investigations involve such cases as contaminated water supplies or food and feed products. These types of investigations require competent laboratory support to determine extent of contamination, source of contamination, and corrective steps to be taken.

ARKANSAS PESTICIDE INVESTIGATIONS, 1970

In determining the who, what, where, when, and how of pesticide poisonings under actual field conditions, it is usually not possible to follow an established "Rule of Thumb". The major factor contributing to pattern disruption is the time lapse between the occurrence of the accident and the receipt of initial information by the investigator. It is usually during this interval that valuable clues are lost or destroyed which, in many instances, leaves elements of doubt in the ultimate verdict.

In Arkansas last year we had a number of pesticide-related accidents which required investigation, most of them fragmentary in nature. Two of them were quite unique and are typical of problems encountered in new state programs. On Saturday, May 30, 1970, an adult male visited the office of a private physician in Monticello, Arkansas, complaining of backache, severe diarrhea, headache, and vomiting. The symptoms indicated a virus infection and the physician prescribed antibiotics.

On Monday, June 1, two adult males, separately visited the same physician's office complaining of "all-over" aching, vomiting, diarrhea, stomach cramps, chest constriction, giddiness, and peeling of the epidermis. These men were also treated for a virus infection.

On Tuesday, June 2, another adult male with essentially identical symptoms visited the same physician and it was here that the doctor became suspicious of something other than a virus infection. These men were all friends of the physician and he began to ask questions regarding their recent activities, particularly with reference to food they had eaten.

It developed that a part-time rancher held a roundup on May 24 for the purpose of inoculating, worming, and spraying his small herd of cattle. Nine men had actively participated in the operation and the rancher's wife prepared a meal for the group.

The physician contacted the other five men by phone and learned that they were experiencing similar symptoms, but to a lesser degree. He first suspected the food, but upon investigation found that a number of other people had eaten the same food without adverse effects. The cattle spray then became the number one suspect.

The product used to spray the animals was Del-Tox, manufactured by Wm. Cooper and Nephews. The Poison Control Center in Little Rock was contacted and the insecticide was found to contain Delnav, the Hercules trade name for dioxathion, a toxic organophosphate. The symptoms manifested by the workmen were confirmed to be similar to those listed for organophosphate poisonings, and atropine was recommended as the antidote agent.

The four men who visited the physician were called in and given atropine. Blood samples of the two most severe cases were forwarded to a laboratory in Monroe, Louisiana, for cholinesterase determination. Another victim was attended by his personal physician who also administered atropine. Two additional victims had severe diarrhea, backaches and giddiness, but would not visit a physician. The remaining two men experienced only slight symptoms and did not receive treatment.

The State Department of Health was not contacted until June 9, ten days after the first victim visited a physician and fifteen days after exposure. An investigation was immediately initiated for the purpose of confirming this physician's suspicions.

It was learned that the cattle were individually inoculated in a chute and released into a small holding pen. When the pen was full of animals, the Delnav insecticide solution was applied to the animals as a very coarse spray, minimizing the occurrence of airborne droplets. The cattle were thoroughly wet and a certain amount of the spray fell to the ground. Only one man was required to apply the insecticide and the remaining eight individuals waited nearby.

The insecticide concentrate was diluted with water according to recommendations on the label and a total of forty-five gallons of the diluted spray solution was used on approximately two hundred cattle. The weather was hot and humid with very little movement of air.

All of the men experienced burning sensations of the exposed skin during the day, particularly the face. Seven of the nine exposed to the spray later experienced peeling of the skin similar to that resulting from sunburn. All nine men had backaches, diarrhea, bronchial disorders, and giddiness. The cattle, including very young calves, demonstrated no ill effects from the insecticide application.

The men who received atropine treatment responded favorably and recovered satisfactorily. Those who did not receive medication apparently have, in time, returned to normal.

All nine men took baths and changed clothing after the roundup. Cleanliness did not appear to be a factor. All were advised to make sure that hats and boots were thoroughly cleaned or to discard them.

Delnav has been found to be a slow acting or reacting organophosphate from the standpoint of toxicology. Poisoning victims respond to atropine treatment but not to 2-PAM.

By the process of elimination it was determined that Delnav (dioxathion) was the causative agent for the illnesses experienced by these nine men.

On Sunday, May 10, 1970, the Arkansas Game and Fish Commission received a report that a severe fish kill was occurring in a drainage canal, Canal #43, in Desha County, Arkansas. Game wardens traced the trail of dead and dying marine life to the headwaters of Wells Bayou, a tributary of Canal 43. The headwaters of Wells Bayou is a combination minnow and rice farm. Dead fish were observed in one of the minnow ponds. By Wednesday morning, May 13, this "death wave" had moved forty-four (44) miles downstream, through a small lake and into the headwaters of lower Lake Chicot in Chicot County, Arkansas, leaving dead fish, snakes, turtles, and crayfish in its wake.

The Arkansas Pollution Control Commission entered the picture on Monday, May 11, and they immediately interviewed the fish farmer and learned that he had sterilized a minnow pond with sodium cyanide and had pumped the residue into Wells Bayou on May 8 and 9. He had also sprayed his rice with propanil. The Arkansas Pollution Control Commission issued a news article on May 13 advising the public that the fish were not fit for human consumption nor should cattle be allowed to drink the affected water. In the meantime, Arkansas Pollution Control Commission biologists took water samples but could not detect any cyanide.

In cooperation with the Arkansas Pollution Control Commission, the Pesticide Project initiated an investigation. Water samples secured from various points along the watercourse were found to contain varying amounts of the pesticide, endrin. The Arkansas Pollution Control Commission chemists also found comparable amounts of endrin in water samples.

An interview on May 15, with the fish farmer confirmed that that he had pumped water containing remnants of sodium cyanide into the drainage ditch but that he did this each time he drained and cleaned a pond. He had also drained his rice field on May 8 and 9. The only pesticides he admitted using on his rice was aldrin for seed treatment and propanil for weeds.

On Friday, May 15, a few carp were continuing to die in Lake Chicot. Blood samples from these fish were found to contain 87 ppb and flesh samples 622 ppb of endrin. Water samples on this date contained 0. 128 ppb of endrin. On May 17, no more dying fish could be found.

An interview with a local pesticide formulator revealed that endrin was no longer being used on agricultural crops as an insecticide. Certain rice farmers were using it to kill reptiles and rodents around rice fields. Water samples taken where fish were dying contained endrin in sufficient quantity to kill rough fish. The minimum lethal concentration range is 0. 1 ppb to 0. 3 and we were finding 0. 125 to 1. 2 ppb. Mud samples by the Arkansas Pollution Control Commission ranged from 1160 ppb in Wells Bayou to 10. 0 ppb downstream in Canal 43.

Of interest is a sample of water taken in Canal 43, above the mouth of Wells Bayou on May 14. This sample contained 1.44 ppb of endrin. The Arkansas Pollution Control Commission took a water sample from the same area on May 15 and a mud sample on May 20. They contained 1.37 ppb and 1160 ppb of endrin, respectively.

On August 12, 1970, the minnow farmer was found guilty of violating the State Water and Air Pollution Act and was fined $250 for discharging water containing cyanide into a public drainage ditch. The Arkansas Pollution Control Commission had charged that the fish kill was caused by a combination of endrin and cyanide discharged into the canal by the minnow farmer. The court held that there was not enough evidence to prove the farmer responsible for the endrin contamination.

SAMPLING PROCEDURES FOR CHEMICALS IN THE ENVIRONMENT

BY

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FOR THE PROBLEM OF IMPACT OF PESTICIDES ON THE ENVIRONMENT TO BE PROPERLY UNDERSTOOD ONE MUST KNOW WHERE THESE CHEMICALS ARE, WHAT THEY ARE, HOW MUCH AND WHETHER THE LEVELS ARE OF BIOLOGICAL SIGNIFICANCE. IT FALLS THEN UPON THE CHEMIST TO DETERMINE THE ANSWER TO MOST OF THESE QUESTIONS BY CHEMICAL ANALYSIS. THE SAMPLING DESCRIBED IN THIS DISCUSSION IS FOR THE PURPOSE OF EPIDEMIOLOGY STUDIES AND IS NOT TO BE USED FOR OFFICIAL SAMPLES FOR REGULATORY PURPOSES AS REGULATORY SAMPLES REQUIRE AUTHENTICATION TO PERMIT THEM TO STAND UP IN COURT.

THE REASON THIS COURSE IS GIVING A WHOLE HOUR TO THE PROBLEM OF SAMPLING IS BECAUSE OF THE IMPORTANCE ATTACHED TO GETTING THIS ASPECT OF THE PROBLEM DONE RIGHT. IF SAMPLES TAKEN ARE NOT REPRESENTATIVE OF THE SUBJECT PROBLEM AREA THEN THE RESULTS OF ANALYSIS ARE WORSE THAN MEANINGLESS, THEY ARE MISLEADING. IF THE CHEMICAL ANALYSIS IS NOT DONE RIGHT IT CAN EASILY ERR BY AN ORDER OF MAGNITUDE WHICH IS THE DIFFERENCE BETWEEN BIOLOGICAL SIGNIFICANCE OR NOT. AND LASTLY, IF THE IDENTIFICATION IS WRONG A SERIOUS SITUATION CAN BE CREATED, PARTICULARLY, IF THE REASON FOR THE STUDY IS A PROBLEM IN HUMAN HEALTH.

LET ME GIVE SOME EXAMPLES. IN A RECENT EPISODE OF POISONING IN SAUDIA ARABIA, PARATHION WAS INDICATED TO BE THE CAUSE BY PHYSICIANS ON THE SPOT. WHEN SAMPLES WERE RECEIVED AT THIS LABORATORY NO PARATHION COULD BE DETECTED IN ANY AMOUNT LET ALONE IN AMOUNTS SUFFICIENT TO CAUSE ILLNESS. IN FACT, IN THE FIRST SAMPLES RECEIVED NOTHING WAS FOUND TO INDICATE THE CAUSE. FINALLY, SAMPLES WERE RECEIVED FROM ANOTHER AREA. THEN THE CHEMISTS BEGAN TO GET PESTICIDE RESPONSE. THESE SAMPLES CAME FROM SACKS OF FLOUR WITH WHAT LOOKED LIKE OIL ON IT. FLOUR FROM CLOSE TO THE OIL SPOT

RAN MANY THOUSANDS OF PARTS PER MILLION ENDRIN. DEEPER INTO THE SACK THE LEVELS DIMINISHED. BUT IMPORTANTLY THE LEVELS WERE HIGH ENOUGH TO ACCOUNT FOR THE ILLNESS. THEN WHEN TISSUE AND FLUIDS FROM THE ILL PERSONS WERE EXAMINED ENDRIN WAS ALSO FOUND IN LEVELS HIGH ENOUGH TO ACCOUNT FOR THE ILLNESS.

IF ONLY THE FIRST SAMPLES HAD BEEN RECEIVED, SAMPLES AIMED AT PROVING THE POINT OF THE ON-THE-SPOT DIAGNOSIS, THEN THE CAUSE OF THE ILLNESS WOULD NOT HAVE BEEN FOUND IN TIME TO PREVENT MORE DEATHS AND ILLNESS.

A WHILE BACK I VISITED A REGULATORY OFFICIAL WHO CONFIDED IN ME ON ONE OF HIS PROBLEMS. HE WAS FINDING ALDRIN IN SOME OF HIS BIOLOGICAL SAMPLES BUT NO DIELDRIN. I ASKED HIM IF HE HAD CONFIRMED HIS ANALYSIS AS PERHAPS THE SIGNAL HE WAS GETTING COULD BE SULFUR. A LOOK OF CONSTERNATION CROSSED HIS FACE. HE SAID NO, HE HAD JUST USED G. C. THINKING THIS WAS SPECIFIC ENOUGH. SUBSEQUENT WORK SHOWED THE COMPOUND RESPONSIBLE FOR THE FALSE ANALYSIS TO BE SULFUR. THIS SAVED A VERY NASTY SITUATION THAT COULD HAVE LANDED IN COURT TO THE EMBARRASSMENT OF ALL CONCERNED.

ONE OF THE MOST COMMON ERRORS IN ANALYSIS IS THE PROBLEM OF GETTING THE DECIMAL POINT IN THE RIGHT PLACE. RECENTLY WE WERE ASKED TO ASSIST IN THE ANALYSIS OF MILK FOR DDT CONTAMINATION. A COMMERCIAL LAB USING NON-APPROVED METHODS HAD REPORTED LEVELS AS HIGH AS 4 PPM AND RESULTED IN A FARMER'S MILK BEING DUMPED. OUR ANALYSIS SHOWED THE HIGHEST LEVELS TO BE 1/10 OF THIS AND MANY SAMPLES TO BE SO LOW AS TO BE OF NO SIGNIFICANCE. I HOPE NOW THE FARMER CAN BE BACK IN BUSINESS.

LET ME THEN GIVE SEVERAL GENERAL RULES FOR SAMPLING:

1. NEVER TAKE A COMPOSITE SAMPLE UNLESS THE SUBJECT AREA TO BE SAMPLED IS KNOWN TO BE UNIFORMLY CONTAMINATED.

2. TAKE A NUMBER OF SAMPLES FROM THE SUBJECT AREA THAT WOULD BEST

REPRESENT POSSIBLE AREAS OF CONTAMINATION.

3. TAKE THE SAMPLES IMMEDIATELY, WHEN REASON FOR CONCERN IS APPARENT. IT MAY BE TOO LATE - LATER.

4. LABEL THE SAMPLES WITH ALL THE INFORMATION IMMEDIATELY. YOU MAY FORGET LATER.

5. PRESERVE THE SAMPLES WITH WHATEVER MEANS ARE NECESSARY. THIS MAY BE REFRIGERATION, FREEZING, FORMALDEHYDE OR SOLVENT.

6. MAKE SURE THE MEANS OF PRESERVATION IS COMPATIBLE WITH SUBSEQUENT ANALYSIS. SAMPLES OF CRAB EATER SEALS AND PENGUINS FROM THE ANTARCTIC WERE SHIPPED BACK TO THIS COUNTRY WRAPPED IN PLASTIC. AS A RESULT THE REPORTED LEVELS OF DDT ARE QUESTIONABLE DUE TO THE PLASTICIZER IN THE PLASTIC. DON'T PRESERVE SAMPLES TO BE USED FOR CHLORINATED HYDROCARBON ANALYSIS WITH CHLOROFORM. DON'T PRESERVE SAMPLES FOR PHOSPHATE ANALYSIS WITH FORMALDEHYDE. IF YOU DON'T KNOW WHAT ANALYSIS WILL BE REQUIRED, REFRIGERATION IS YOUR BEST BET.

7. TAKE A LARGE ENOUGH SAMPLE. TOMORROW WILL BE TOO LATE TO GET MORE.

8. BE PREPARED TO TAKE SAMPLES. HAVE SAMPLING TOOLS NEEDED, KNIVES, SCISSORS, TROWELS, SPOONS, ETC. HAVE SUITABLE BOTTLES FOR SAMPLES. TISSUE SAMPLES CAN BE WRAPPED IN ALUMINUM FOIL. BE PREPARED.

9. LABEL ALL SAMPLES.

10. WRITE A DESCRIPTION OF THE SITUATION AS THE INVESTIGATOR SEES IT AT TIME OF SAMPLING. IT IS NOT UNUSUAL FOR THE COST OF ANALYSIS IN PARTICULAR INVESTIGATIONS TO RUN $10,000. THIS EXPENDITURE SHOULD NOT BE JEOPARDIZED BECAUSE THE SAMPLER IS TOO LAZY TO WRITE DOWN THE SITUATION AS HE SEES IT. PROVIDE A CASE HISTORY. THIS IS NEEDED FOR THE CHEMIST TO GET A CLUE AS TO WHAT TO ANALYZE FOR. HE CANNOT POSSIBLY SCREEN FOR THE

million or so compounds that presently contaminate our environment.

11. Get samples to laboratory now. Don't wait two weeks while you talk the situation over.

Procedures for Taking Samples

It should not be necessary to talk about the taking of autopsy samples. Yet, the fact remains that we seldom get autopsy samples from poisoning cases in this laboratory which are really satisfactory. Mostly it is a problem of labeling and packing. Instead of the pathologist being prepared for the job, invariably he uses what containers he has on hand and preserves the sample by whatever means is convenient. We have had samples come in used containers, washed - we know not how. We have had samples for chlorinated hydrocarbon analysis shipped in carbon tetrachloride.

One and two ounce salve bottles are satisfactory for most autopsy samples including fecal matter, urine and stomach contents. I cite the latter because in the case of poisoning from unknown cause, they all should be sent to the laboratory. Generally, two ounces is the maximum of any sample needed for analysis. Don't try to figure out how little you can send. Rather, send as much as possible up to this maximum

In case food is implicated in an incident send as much as possible. Send the whole meal of the person, or the whole sack of flour. If for legal or other reasons this is not possible, the lab must get samples representative of all that the subject has eaten.

In the case of poisoning from unknown cause around the house, look to all the areas the victim could have been in the 12 hours prior to

ILLNESS. LOOK AT WATER GLASSES, EMPTY CONTAINERS, DISCARDED ITEMS SUCH AS BAGS, BOTTLES OR THE LIKE. LOOK IN THE KITCHEN, STORAGE AREA, GARAGE, CELLAR, OUTBUILDINGS, AND BATHROOM. DON'T NEGLECT THE POWDER AROUND THE KITCHEN CABINETS. DON'T FORGET TO MENTION IF ANY INSECTICIDE HAS BEEN USED IN THE AREA WITHIN THE LAST THREE MONTHS. IT MAY BE NECESSARY TO SUPPLY FABRIC FROM FURNITURE IN A ROOM WITH AN UNUSUAL OR PESTICIDAL ODOR. BACKING FROM A RUG MAY BE USEFUL. AN ITEM OF CLOTHING WITH UNUSUAL ODOR OR STAIN SHOULD BE SENT TO THE LABORATORY. IT CAN ALWAYS BE RETURNED IF NEGATIVE.

IN CASE OF EXPOSURE IN A YARD OR FIELD, SPECIAL VIGILANCE IS NEEDED. THE AREA SHOULD BE SEARCHED CAREFULLY FOR OIL SPOTS OR AREAS THAT LOOK DIFFERENT FROM THE SURROUNDINGS. THESE CAN BE SAMPLED BY USING A SAMPLING TOOL MADE FROM A TOMATO SOUP CAN OR SIMILAR CONTAINER. CUT BOTH TOP AND BOTTOM OUT EVENLY. WASH WELL AND REPEATEDLY. RINCE IN CLEAR WATER. PRESS THIS CAN IN SUSPECT AREA TO DEPTH OF 1 1/2 - 2 INCHES AND REMOVE FROM SOIL. PUNCH CORE TAKEN INTO NEW QUART MASON JAR. TAKE SEVERAL MORE CORES FROM SAME AREAS. SEAL JAR AND SEND TO THE LABORATORY AFTER CAREFUL MARKING TO INDICATE WHERE SAMPLE WAS TAKEN, WHEN, BY WHOM, AND NUMBER AND DEPTH OF CORES.

IF THE ENVIRSONS OF A HOUSE ARE SUSPECT, A NUMBER OF CORE SAMPLES CAN BE TAKEN ALL AROUND THE HOUSE AND EVEN UNDER THE HOUSE. IF IT IS KNOWN THE AREA WAS TREATED UNIFORMLY THEY CAN ALL BE PUT TOGETHER. OTHERWISE, MAKE SEPARATE CONTAINERS OF THE NORTH, EAST, SOUTH, AND WEST SAMPLES, AS WELL AS A SEPARATE SAMPLE FROM UNDER THE HOUSE.

IN CASE WATER CONTAMINATION IS SUSPECTED, PROVIDE A GALLON SAMPLE, AT LEAST, OF THE SUSPECT SOURCE. IF CONTINUING CONTAMINATION IS SUSPECTED, PROVIDE A NUMBER OF SUBSEQUENT SAMPLES. A CUP CAN BE USED TO FILL THE CONTAINERS FROM A SHALLOW SOURCE. IN A DEEP SOURCE, TAKE A SURFACE

SAMPLE, A BOTTOM SAMPLE AND INTERMEDIATE SAMPLE. THIS CAN BE DONE BY SUBMERGING THE CLOSED SAMPLE CONTAINER TO THE REQUIRED DEPTH AND THEN REMOVING THE CLOSURE. WHEN FULL, CLOSE THE CONTAINER REMOVE, DRY AND LABEL. IN A LARGE BODY OF WATER THIS WOULD HAVE TO BE REPEATED MANY TIMES TO BE REPRESENTATIVE. DO NOT USE PLASTIC FOR WATER CONTAINERS. ALWAYS USE CLEAN GLASS CONTAINERS.

SOMETIMES CONTAMINATION ON A WALL OR DUCT OR OTHER SURFACE IS SUSPECTED. IN THIS CASE, GET A PACKAGE OR STERILE COTTON WOOL, SOME MEDICAL ALCOHOL OR ACETONE AND PLASTIC GLOVES AS USED BY SURGEONS FOR THROW AWAY PURPOSES. WEARING THE GLOVES, WASH THE SUSPECT AREA WITH SWABS OF COTTON AND SOLVENT USING CARE NOT TO LET SOLVENT SQUEEZE OUT OF THE SWAB. PLACE USED SWAB IN PINT MASON JAR. REPEAT ON ADJACENT AREA. WHEN LABELING BOTTLE RECORD WHERE SAMPLE WAS TAKEN AND BY WHOM, HOW IT WAS SAMPLED AND HOW LARGE AN AREA.

IN TABLE 1 PRESENTED INFORMATION ON THE TAKING OF ENVIRONMENTAL SAMPLES ARE SHOWN, I.E. SIZE OF SAMPLE, PACKING, STORAGE, PRESERVATIVES, AND OTHER INFORMATION PERTINENT TO THE PROBLEM.

TABLE I Environmental Sampling

SAMPLE	SIZE OF SAMPLE	PACKING *	STORAGE	PRESERVATIVE	OTHER INFORMATION
		SAMPLING OF WATER FOLLOWING INCIDENT			
private well	1 gallon	glass	ambient	none	description of well date
municipal pre filter at filter treated	1 gallon ea.	glass	ambient	none	note where and when taken
river	1 gallon	glass	ambient	none	detailed location of sampling site and date
lake	1 gallon	glass	ambient	none	detailed location of sampling site and date

Accompanying each set of samples should be a complete description of incident and all pertinent information to guide laboratory director in making analysis.

SAMPLING OF TISSUE AT AUTOPSY

fat	1 to 5 gms	glass bottle or aluminum foil	frozen or	10% Formaldehyde	name of subject site of sample sample size date, cause of death
liver lung brain gonads spleen muscle etc.	1 to 5 gms	glass bottle or aluminum foil	frozen	not acceptable	name of subject name of tissue sample size date, cause of death

* Where glass containers are specified they should be fitted with teflon or aluminum lining.

TABLE I Environmental Sampling (Cont.)

SAMPLE	SIZE OF SAMPLE	PACKING	STORAGE	PRESERVATIVE	OTHER INFORMATION
		SAMPLING OF BODY FLUIDS			
urine for chlorinated hydrocarbons	**25 ml of 24 hr. sample if possible	glass	ambient	1/10% Formaldehyde	name of subject description whether 24 hr. or not.
urine for phosphates	**25 ml of 24 hr. sample if possible	glass	frozen	none	name of subject description, whether 24 hr. or not.
blood for chlorinated hydrocarbon	1-5 ml plasma	glass tube oxaloted	frozen	none	name of subject reason for analysis date, physician
blood for phosphates	1-5 ml whole blood	glass tube oxaloted	frozen	none	name of subject reason for analysis date, physician
blood for cholinesterase	1-5 ml plasma	glass tube heparinized	refrigerated	none	name of subject reason for analysis date, physician
	1-5 ml red cells	glass tube heparinized	refrigerated	none	name of subject reason for analysis date, physician

A complete case history should be provided with all human samples.

TABLE I Environmental Sampling (Cont.)

SAMPLE	SIZE OF SAMPLE	PACKING	STORAGE	PRESERVATIVE	OTHER INFORMATION
			OTHER SAMPLING		
soil	1 lb.	glass or metal can	ambient	none	description of site, amount sampled, by whom and why.
sediment	1 lb.	glass or metal can	ambient	none	description of site, amount sampled, by whom and why.
wildlife birds mammals or reptiles	20 gms muscle (20 gms fat if possible)	glass	frozen	none	detailed description of sampling site name of animal approx. age if known by whom and why.
fish	20 gms tissue	glass	frozen	none	detailed description of sampling site name of animal approx. age if known by whom and why.

Analysis of one animal, fish or bird will generally tell, but little. Enough animals should be sampled to provide a crossection exposure picture of the incident but certainly never less than 10 subjects.

TABLE I Environmental Sampling (Cont.)

AIR SAMPLING

Sampling of air requires sophisticated equipment and methods. Consult State Services Section for information.

Other Sampling

Many other types of sampling are occasionally required such as grain, feed, flour, food or other types of samples representing human or animal exposure. It is highly important in such cases to inspect carefully the material to be sampled in order to detect possible areas of contamination. Sometimes only one sack in a shipment will show an oily spot of contamination, or the colored grain denoting seed treatment. Samples should be drawn both from suspect and non-suspect areas and so labeled. If in doubt call the laboratory for guidance.

Labeling and Shipping

Without proper labeling or shipping all the care and trouble of taking the samples is wasted. Be sure the label is explanatory and well attached. Ship samples on a Monday that they arrive during the week and not over the weekend where they might sit in a hot airport terminal and spoil. If the samples are worth taking they are worth packing well and a little extra dry ice or other refrigerant.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL COMMUNICABLE DISEASE CENTER
PESTICIDES PROGRAM
ATLANTA, GEORGIA 30333

FORM APPROVED
BUDGET BUREAU NO. 68-R1614

157

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1. D100987

COMMUNITY STUDIES PROJECT ON PESTICIDES
ACUTE EXPOSURE RECORD

PARTICIPANT'S NAME

2. PROJECT CODE # __ __ 3. GROUP ID __

4. AMA ID # __ __ __ __ __ __ __ __ __ __

PARTICIPANT'S ADDRESS *(include zip code)*

EMPLOYER'S ADDRESS *(include zip code)*

6. *(D060)* 1 ☐ URBAN 2 ☐ RURAL 3 ☐ UNKNOWN

DATE OF BIRTH __/__/__ | PHONE | SEX | RACE

5. INTERVIEW DATE __/__/__

7. MARITAL STATUS: 1 ☐ Married 2 ☐ Widowed 3 ☐ Divorced 4 ☐ Single

INTERVIEWER'S NAME

EMPLOYER

8. SOURCE OF DATA: 1 ☐ Participant 2 ☐ Employer 3 ☐ Relative 4 ☐ Other *(If other than participant, give name)* ____________

9. CURRENT OCCUPATION: *(D010)* CODE (INDEX I) __ __

NUMBER OF YEARS __ __ *(Report to nearest year)*

10. CHIEF COMPLAINT: *(D020)*
(Mark (x) by any symptoms which occurred as part of the chief complaint.)

CODE
00 ☐ none
01 ☐ malaise
02 ☐ fatigue
03 ☐ confusion
04 ☐ headache
05 ☐ nervousness
06 ☐ hyperirritability
07 ☐ light-headedness
08 ☐ fainting
09 ☐ dizziness
10 ☐ dermatitis
11 ☐ coma, unconsciousness
12 ☐ skin flushing
13 ☐ increased sweating
14 ☐ cyanosis
15 ☐ blurred vision
16 ☐ increased tearing
17 ☐ rhinitis
18 ☐ nasal stuffiness
19 ☐ increased salivation
20 ☐ tightness in chest
21 ☐ difficult breathing
22 ☐ palpitations
23 ☐ nausea
24 ☐ vomiting
25 ☐ abdominal pain, cramps
26 ☐ diarrhea
27 ☐ muscular weakness
28 ☐ tremor, fasciculations
29 ☐ convulsions
30 ☐ paresthesiae
31 ☐ other (specify) ____________
32 ☐ fever

PRESENT ILLNESS

11. CASE TYPE: *(D030)* *(Mark (x) in block by appropriate answer)*
1 ☐ Accidental-home
2 ☐ Nonaccidental-occupational
3 ☐ Accidental-occupational
4 ☐ Suicide or attempted suicide
5 ☐ Homicide
6 ☐ Other ____________

12. DATE AND PERIOD OF EXPOSURE: *(D040)*
began (date) __/__/__ (time) _____
ended (date) __/__/__ (time) _____ *(Use 24 hour clock)*

13. SUSPECTED AGENT(S): *(list chemical names of pesticides and solvents. If only brand name is available, record and look up chemical name later.)*

NAME	FORM (E.G. DUST, LIQUID, ETC.)	CODE (INDEX II)	APPROX. AMOUNT (IF INGESTED)
	(D050)	_/__/____	mgm
		_/__/____	mgm
		_/__/____	mgm
		_/__/____	mgm
		_/__/____	mgm
		_/__/____	mgm
		_/__/____	mgm

1 69-4 (NCDC)
6-69

14. PROBABLE MAIN ROUTE OF EXPOSURE: *(D060) (Mark (x) in block by appropriate answer)*

1 ☐ oral
2 ☐ dermal
3 ☐ inhalation
4 ☐ combination or other

15. PHRASE WHICH BEST DESCRIBES SOURCE OF AGENT: *(D070) (Mark x) in block by appropriate answer)*

1 ☐ unknown or not applicable
2 ☐ bought in store
3 ☐ bought from door-to-door salesman
4 ☐ chemical taken from work
5 ☐ chemical taken from elsewhere
6 ☐ applied by commercial firm
7 ☐ applied by other person
8 ☐ provided by employer for job
9 ☐ other ______________________

16. WHICH BEST DESCRIBES CONTAINER? *(D080)* *(Mark (x) by one item from each column)*

A

1 ☐ original container, labeled
2 ☐ original container, unlabeled
3 ☐ other container, unlabeled
4 ☐ other container, mislabeled
5 ☐ other (specify ______________________)

B

6 ☐ paper sack or bag
7 ☐ plastic sack or bag
8 ☐ bottle
9 ☐ can or drum
10 ☐ other (specify ______________________)

17. WHICH BEST DESCRIBES STORAGE AREA AT HOME OR AT PLACE WHERE POISONING OCCURRED? *(D090) Mark (x) in one box in each column. (USE ONLY IF QUESTION 11 ABOVE INDICATES HOME CASE TYPE)*

A

1 ☐ locked
2 ☐ unlocked

B

3 ☐ kitchen
4 ☐ bathroom
5 ☐ closet
6 ☐ garage, shed, etc.
7 ☐ other (specify ______________________)

C

8 ☐ below ground or floor level
9 ☐ 1–4 feet above ground or floor level
10 ☐ 4–8 feet above ground or floor level
11 ☐ 8+ feet above ground or floor level

18. WHICH CIRCUMSTANCES CONTRIBUTE TO PESTICIDE INTOXICATION IN THE OCCUPATIONALLY-EXPOSED? *(D100) Mark (x) for items which best describes. (USE ONLY IF QUESTION 11 ABOVE INDICATES OCCUPATIONAL CASE TYPE)*

1 ☐ unknown
2 ☐ spillage
3 ☐ equipment malfunction
4 ☐ poor ventilation of work environment
5 ☐ poor application techniques, or poor work practices
6 ☐ drift
7 ☐ too early re-entry after fumigation
8 ☐ intentional (specify ______________________)
9 ☐ other (specify ______________________)

19. WHICH CIRCUMSTANCES CONTRIBUTE TO PESTICIDE INTOXICATION? *(D110) Mark (x) for items which best describe (THIS IS TO BE FILLED OUT IN EVERY INSTANCE)*

1 ☐ unknown
2 ☐ ate or drank from container
3 ☐ ate bait
4 ☐ ate contaminated soil
5 ☐ drank contaminated water
6 ☐ other oral source (specify ______________________)
7 ☐ handled container or pesticide
8 ☐ handled contaminated object (e.g. glove) (specify ______________________)
9 ☐ exposed to contaminated soil or water
10 ☐ other dermal source (specify ______________________)
11 ☐ inhalation when foam or sponge rubber furniture was present
12 ☐ inhalation when change in ambient temperature was causally related (specify ______________________)
13 ☐ other inhalation (specify ______________________)

20. DID THIS PATIENT TAKE ANY OF THE FOLLOWING DURING THE LAST WEEK? *(D120)* 1 ☐ Yes 2 ☐ No 3 ☐ Unknown

(if yes, mark (x) in box by appropriate items below, and provide requested information)

	NAME	QUANTITY/UNITS, FREQUENCY (HRS.)	DATE AND TIME LAST TAKEN	
			MO. DA	TIME (use 24 hour clock)
alcohol		(D121)	__/__	____
sedatives		(D122)	__/__	____
narcotics		(D123)	__/__	____
phenothiazine tranq.		(D124)	__/__	____
carbamate tranq.		(D125)	__/__	____
		(D126)	__/__	____
		(D127)	__/__	____

21. HOW LONG HAD PESTICIDES BEEN AVAILABLE AT EXPOSURE SCENE? *(D130)*

1 ☐ not applicable or unknown
2 ☐ hours
3 ☐ days
4 ☐ weeks
5 ☐ months
6 ☐ years

2 ☐ rubber gloves
3 ☐ mask or respirator
type ____________
5 ☐ long sleeves
6 ☐ coveralls
7 ☐ apron
9 ☐ goggles
10 ☐ other (specify ____________)

23. WHICH OF THE FOLLOWING FIRST-AID MEASURES WERE INSTITUTED IMMEDIATELY? *(D130)*

1 ☐ none
2 ☐ change clothes
3 ☐ wash exposed area with soap and water
4 ☐ wash exposed area with other solvent
5 ☐ bath or shower
6 ☐ vomiting induced (method ____________)
7 ☐ gave antidote (specify ____________)

24. HOW MANY HOURS ELAPSED BETWEEN EXPOSURE AND BEGINNING OF COMPLAINTS?

(D160) __ __ hrs. *(D161)* __ __ min.

25. HOW MANY HOURS HAD COMPLAINTS BEEN APPARENT BEFORE MEDICAL ATTENTION RECEIVED?

(D170) __ __ hrs. *(D171)* __ __ min.

26. WHAT COMPLAINTS (SYMPTOMS) OTHER THAN THOSE IN THE CHIEF COMPLAINT WERE ASSOCIATED WITH THIS ILLNESS? *(D180)*

00 ☐ none
01 ☐ malaise
02 ☐ fatigue
03 ☐ confusion
04 ☐ headache
05 ☐ nervousness
06 ☐ hyperirritability
07 ☐ light-headedness
08 ☐ fainting
09 ☐ dizziness
10 ☐ dermatitis
11 ☐ coma, unconsciousness
12 ☐ skin flushing
13 ☐ increased sweating
14 ☐ cyanosis
15 ☐ blurred vision
16 ☐ increased tearing
17 ☐ rhinitis
18 ☐ nasal stuffiness
19 ☐ increased salivation
20 ☐ tightness in chest
21 ☐ difficult breathing
22 ☐ palpitations
23 ☐ nausea
24 ☐ vomiting
25 ☐ abdominal pain, cramps
26 ☐ diarrhea
27 ☐ muscular weakness
28 ☐ tremor, fasciculations
29 ☐ convulsions
30 ☐ paresthesiae
31 ☐ other (specify ____________)
32 ☐ fever

TREATMENT AND CLINICAL COURSE *(present illness)*

27. NAME OF ATTENDING PHYSICIAN

____________ MD

PHYSICIAN'S ADDRESS *(include zip code)*

____

29. NAME OF HOSPITAL

____________ No. days hospitalized *(D190)* __ __ __

0. TREATMENT

Treatment is presumed to include the usual supportive measures such as airway, oxygen, necessary IV fluids, etc. Hence these need not be mentioned unless their omission has contributed to the course. The medicine should include all pertinent ones, but single doses of aspirin, etc., may be omitted.

The physician need not detail each single dose as an individual listing. Rather, each change in schedule should be noted. The response should be either clinical or pharmacological and should be descriptive rather than a value judgment, for example:

EXAMPLE:

MEDICINE	CODE (INDEX III)	DOSAGE	TOTAL AMOUNT	RESPONSE
Atropine	1 4	0.8 mgm IV q min x 8	6.4 mgm	• pulse, dilated pupils
Atropine	1 4	0.8 mgm IV q 1 hr x r	3.2 mgm	recovered consciousness
2-PAM	4 1	1 gm IV slowly	1000.0 mgm	no clinical;

MEDICINE	CODE (INDEX III)	DOSAGE	TOTAL AMOUNT	RESPONSE
(D200)	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	
	— —		— — — — . — mgm	

(CDC)

31. OUTCOME:

(D210) 1 ☐ fatal 2 ☐ recovered 3 ☐ residual damage

32. FINAL DIAGNOSIS:

(D220) 1 ☐ pesticide intoxication 2 ☐ solvent intoxication 3 ☐ drug intoxication 4 ☐ other

33. CONFIRMATION OF ETIOLOGIC AGENT:

EXAMPLE

AGENT	CODE (INDEX II)	SOURCE	CODE	CONCENTRATION	UNITS	METHOD
Parathion	8/04/_290	Container	6	5000	ppm	EC
Parathion	8/04/_290	Vomitus	1	500	ppm	U/V
PNP	0/07/_478	Serum	2	2	ppm	Elliott
PNP	0/07/_478	Urine	3	45	ppm	Elliott

AGENT	CODE (INDEX II)	SOURCE	CODE	CONCENTRATION	UNITS	METHOD
(D230)	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	
	_/__/_____		_		ppm	

34. HAS SUBJECT HAD A PREVIOUS EPISODE OF PESTICIDE POISONING? *(D240)* 1 ☐ yes 2 ☐ no 3 ☐ unknown
(if yes, give date, etc., below)

Dates (mo./yr.)	Has PHS 1.165-4, ACUTE EXPOSURE RECORD, been completed for each episode? Yes	No
(D241) __/__	1 ☐	2 ☐
__/__	1 ☐	2 ☐
__/__	1 ☐	2 ☐
__/__	1 ☐	2 ☐

***If PHS 1.165-4 has not been completed complete one now.**

35. WERE OTHER WORKERS OR FAMILY MEMBERS ALSO EXPOSED OR ILL? *(D250)* 1 ☐ Yes 2 ☐ No
How many? __ *(Give details below)*

36. CONCLUDING REMARKS: *(D260)* 1 ☐

DEVELOPING LABORATORY COMPETENCE

Bill L. Stevenson, Ph.D.

The presence of pesticides in human tissues and the environment throughout the world attests to the almost universal application of and exposure to these materials. Even though much is known generally, a need exists in many geographical areas to provide a competent basis for the detection and evaluation of pesticide levels within specific localities before gross environment and physiological responses are manifested. Thus, establishment of a laboratory to fulfill this need appears to be essential to a basic knowledge of identifying current and potential public health problems as well as protecting the environment from unanticipated contamination.

In general, the Division of Pesticide Community Studies, State Services Branch, in cooperation with the Perrine Primate Research Branch, has developed four major broad objectives to improve laboratory competence in pesticide residue analysis.

a. Nominating for attendance at the course, "Principles and Practice of Analytical Chemistry of Pesticides," at least one chemist who has, or on his return will assume, some responsibility for pesticide analysis in health related problems.

b. Encouraging attendance of appropriate personnel at other selected specialized training courses on the subject as relevant to the purpose of the contract.

c. Updating laboratory equipment by outlining a plan for modernizing laboratory equipment so that it will be adequate for performing the necessary analytical tests for support of a pesticides program.

d. Laboratory competence may be evaluated by initiating a method to provide for comparability of data by establishing an intra-laboratory quality control program and by participating in an inter-laboratory control program sponsored by a reference laboratory.

The training facility located in the Perrine Primate Research Center is well known for its excellence of instruction and superior staff. Training at this facility is designed to produce pesticide residue chemists capable of analyzing samples of human tissues and body fluids, environmental media, and food products, for organophosphate pesticides and their metabolites. Students are trained on equipment which will provide the experience they require to produce dependable qualitative and quantitative data[1].

To update or establish a laboratory facility for pesticide residue analysis is a complex endeavor since each laboratory will encounter its own particular problems; however, some specific points to be considered are:

2. Level of expediency desired.
3. Single or multiple agency laboratories.
4. Physical location of a laboratory.
5. Assignment of responsibilities.

Of primary importance is the consideration of legal responsibilities delegated to a laboratory. In general, most states have legislation similar to the Federal Food and Drug laws. Many states are proposing new legislation directed specifically toward pesticides; an example is Montana where items must be monitored to insure consumers that products are not adulterated by foreign material and that they meet labeling requirements. In addition to that responsibility, provisions are made within the law to monitor crops, water and other parts of the environment.

A budget and proposed laboratory needs to support pesticide legislation in Montana have been proposed in the following manner.[2]

The Department of Health will handle the monitoring of pesticide products for adulterants and mislabeling. The Department of Agriculture will administer the use and application portion of the law, and handle complaints received on suspected misapplication of pesticides. As outlined in the budgets these two pesticide monitoring programs will adequately provide the necessary laboratory facilities. However, additional consideration is necessary for the establishment of pesticide laboratory facilities for monitoring not directly related to the proposed law. The areas of responsibility delegated to various departments in the state of Montana for pesticide residue analysis are as follows:

Department of Agriculture

Residue analysis on the fee-for-service basis to agriculturalists, soil, etc.

Department of Fish and Game

Monitoring the environment of fish, game, water, and aquatic organisms for pesticides affecting fish and wildlife.

Department of Health

Food and Drug Law (raw agricultural commodities and manufactured food products). Water, air, human tissue, and samples from occupational health programs.

Livestock Sanitary Board

Milk and meat.

Other Departments

Forestry, Entomology and various other agencies are involved in pesticide monitoring; however, these are usually limited to special problems.

An example of a budget for a State Health Department to establish a pesticide laboratory for monitoring such items as food products, water, air, and tissues is shown in attachment A.2/

Laboratories that have initiated internal or intra-laboratory analytical quality-control programs rarely have poor analytical performance. Conversely, laboratories lacking a well coordinated internal quality control program may expect sporadic performances.

There are numerous ways of conducting an internal analytical quality assurance program, and it is doubtful that any one system would be totally suitable for all laboratories. In September, Thompson3/ published a guide for initiating a quality control program adaptable to most laboratory situations, see attachment B.

In the past and possibly more important, in the future, laboratory competency will be recognized as one of the most influential factors for deciding administrative and/or judicial action.

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2. Gingery, G. L. "Progress Report of the State Pesticide Project, Montana State Department of Health, Helena, Montana."

3. Thompson, J. R. "Internal Analytical Quality Control Program," Personal Correspondence, September 8, 1970. Group Leader, Analytical Quality Control, Perrine Primate Research Branch, P.O. Box 490, Perrine, Florida 33157.

Attachment A

Budget Proposal for Establishing a State
Pesticide Laboratory, Montana State Health Department

Building Facilities

- Director Office and Meeting Room
- Offices for Two Secretaries and Files
- Three Offices for Chemists (located near laboratories)
- Library and Staff Meeting Room
- Calculator Room
- Bulk Chemical Storage Room
- Walk in Cooler
- Freezer Room
- Organic Solvent Room (isolated, fire, and explosive proof)
- Balance Room
- Formulation Analysis
  - Storage Room
  - Laboratory
  - Instrumentation
- Residue Analysis
  - Preparation Rooms (2)
  - Laboratory
  - Instrument Room
  - Storage Room

Laboratory would be required to have distilled water source, natural gas, steam source, compressed air, excellent ventilation, and air conditioning, including hoods in the laboratories.

COST OF FACILITY

Land Aquisition		
Preliminary Expenses		
Site Survey		$500
Soil Testing		$500
Administrative and Legal Expenses		$1,000
Furnishings and Special Equipment		$125,000*
Landscaping and Site Development		$8,000
Construction Cost		$150,000
A/E Services		$13,500
Contingencies		$3,000
	TOTAL	$301,600

* This item includes capitol outlay items as required by law. These items are listed on page 4.

Approximate cost per square foot	$33
Square feet of building	5650
Outside dimensions	47' x 120'

Director	$14,000	$14,000
Chemist III - 3	10,800	32,400
Chemist I - 3	8,280	24,840
Laboratory Technician - 4	6,600	26,400
Secretary	600 per month	7,200
Clerk-Typist	420 per month	5,040
SUBTOTAL		$109,880

Surcharge

12%	$1,680.00
12%	3,888.00
12%	2,980.00
12%	3,168.00
10.25%	738.00
10.25%	516.00
	$12,970.60

12,970.60
$122,850.60

EXPECTED SAMPLE LOAD

Law*

Formulation	150 - 300
Complaints	100 - 300
SUBTOTAL	250 - 600

Residue

Soil	50 - 150 x $45	=	$ 6,750
Water	1,000 x $45	=	45,000
Food	2,000 x $35	=	70,000
Air	60 x $50	=	3,000
Human Tissue	50 x $50	=	2,500
Fish and Game	500 x $35	=	17,500
	3,080		$144,750

*Costs of laboratory functions in terms of law is listed under Operations, Page 5.

Capitol Equipment

I-R spectrophotometer and accessories	$13,000
U-V spectrophotometer	12,500
3 dual column gas chromograph and accessories	35,000
1 microcolormetric G. C.	9,500
deep freezes and refrigerators	3,500
Grinding and Blending Equipment	5,500
Atomic Absorption Instrument	10,000
Thin layer equipment	1,500
Hot plates, rack, carts, steam baths, and other small lot apparatus	3,500
Centrifuges - 2	2,500
4 balances	4,000
Bomb calorimeter	1,000
Office equipment	6,000
Vehicle	2,600
Calculators	5,000
TOTAL	$115,100

Operational Costs

Materials and Supplies

Initial Lab Supplies

Glassware	$ 8,000
Chemicals	3,000
Organic Solvents	7,500
Laboratory Hardware	3,750

Travel (instate and out of state)	$3,000
Training	4,000
Maintenance	3,000
Law - chemicals and glassware*	15,000
TOTAL	$47,250

TOTAL INITIAL COSTS - First Year's Operation

Building	$301,600.00
Staff	122,850.60
Samples	144,750.00
Capitol Outlay $115,100*	
Operational Costs	47,250.00
	$616,450.60

* included with building costs

NOTE: Information on the availability of Federal funds for construction of laboratories will be obtained and forwarded to you in the near future.

ATTACHMENT B

Internal Analytical Quality Control Program

Certain checks should be made daily, others on a weekly or monthly basis. Figure 1 outlines the suggested frequency of such instrumental checks.

It is suggested that a written log be maintained for each instrument, recording the following data:

1. Date of installation and serial number of each detector (E.C.) installed (This will also serve as a record for A.E.C. inspection).
2. Background current (BGC) profile furnished by Perrine with each detector.
3. Your own BGC profiles obtained at time of installation of each detector and subsequent profiles (column identity notations should be made).
4. Date of change of pyrometer batteries.

Instrumental malfunction is generally indicated by distorted chromatograms. Attached Figure 2 shows a number of pictorial symptoms of malfunction along with possible causes and remedies.

It is strongly suggested that a record be kept of each GLC column packed and installed in an instrument, logging such information as:

1. Assignment of a column number.
2. Date of packing column.
3. Liquid phase identity and lot number of precoated column packing.
4. Conditioning temperature, flow rate and number of hours.
5. Length and shape of column.
6. Background current obtained on newly installed column and subsequent background current profiles during the life of the column.
7. Date of each silylation of column.
8. Compound conversion data, with dates monitored, and percentage of compound breakdown.

9. Monthly, chromatograph special column evaluation mixture (Figure 3) and record efficiency, absolute and total retention, based on the p,p'-DDT peak.

A. ADHERENCE TO STANDARD ANALYTICAL METHODS.

If reproducible and meaningful data is to be forthcoming from a multi-laboratory system, it is completely essential that uniform methodology be used. It is therefore important that each laboratory adhere in detail to the standard analytical methods. Open channels are established for the consideration of suggested changes in methodology. At no time, however, should any individual summarily introduce method revisions, change to unauthorized GLC columns, alter specified operation parameters, or make any other changes not authorized by the Perrine Analytical Quality Control group. It is highly significant that the vast majority of poor analytical performances on interlaboratory check samples have been performed by laboratories who were deviating in one or more ways from the standard procedures. It is earnestly hoped that whenever difficulty is encountered, it will be called to the attention of the Perrine Quality Control group so that the problem can be defined and eliminated.

B. CAPABILITY OF PERSONNEL TO OBTAIN SATISFACTORY RECOVERIES:

The interlaboratory check sample program wherein the Perrine Quality Control group sends you a sample to analyze is of value to each individual laboratory only in light of the performance turned in by one analyst on infrequent occasions. An internal check sample program, on the other hand, should be in constant use by every laboratory to provide a running measurement of the performance caliber of each bench chemist on the staff. With such a program functioning properly, each staff member can constantly be aware of the strengths and weaknesses in his analytical performance, and most importantly, corrective steps can be taken before a large amount of erroneous data is reported by the laboratory.

A continual, systematic program of procedural recoveries and test samples is necessary to assure high analytical quality. Periodic analysis of a standard sample will be required for adipose tissue and blood serum. Each chemist on the staff who is conducting analyses on these sample materials should participate.

All recovery results from each chemist shall be recorded on the appropriate INTERNAL CHECK SAMPLE table which should be available for examination by all staff members. Labs performing an average of one or more routine analyses per week of a given substrate will make weekly analysis of standard substrate. Those labs making less than one routine analysis per week of a given substrate will analyze the standard substrate each time they have occasion to analyze any corresponding sample substrate, but not less frequently than once each month. As an illustration, if a laboratory is averaging one blood serum analysis every three weeks, the standard serum sample shall be analyzed each time an unknown sample is analyzed. If that laboratory is making 12 analyses per week of adipose tissue, a standard sample of fat shall be run once each week, carrying the analysis of the standard right along with a group of routine samples, giving it no different treatment whatever than is given the routine samples.

If more than one chemist (or technician) is involved in the routine analyses of a given substrate, and if each individual conducts the entire analysis (preparative as well as determinative), then each individual should run a separate standard sample. If, on the other hand, routine analyses are conducted in piecework fashion, with one individual performing the preparative portion and a second individual conducting the chromatography, one determination of the standard sample will suffice as this represents the routine norm for the entire analysis.

Immediately upon completion of each analysis of a standard sample, the results will be recorded on the appropriate INTERNAL CHECK SAMPLE form. Handwriting is sufficient provided it is easily legible. Each participating chemist should have ready access to this record. The laboratory director will be furnished with the results of the Perrine replicate analyses on each standard sample. In the event of any significant deviations from the Perrine mean values, an immediate investigation should be made to determine the reason(s) for the deviation. It is possible of course, that the Perrine results could be in error, but every precaution will be taken to cross-check analytical results before the samples are mailed from Perrine.

When your official quarterly report is prepared, make two photocopies each of the INTERNAL CHECK SAMPLE tables, including one copy of each substrate with the confidential in-house section of the report and mailing the other to the Quality Control group in Perrine (no covering letter needed with the latter copy). It is realized that succeeding quarterly copies will contain some of the same data as reported the previous quarter but there is no objection whatever to this. After the data from all laboratories are compiled, you will be furnished with statistical summaries for comparison of your results with those of all other laboratories.

C. TRAINING, EXPERIENCE AND RESPONSIBILITIES OF PERSONNEL:

A number of the routine functions of the residue laboratory can be carried out by a technician who has been given careful on-the-job training by the chemist. This relieves the chemist to devote his efforts to the more complex problems of instrumentation and interpretation.

In the small laboratory of three to six people, the responsibility rests with each chemist to sufficiently acquaint himself with his analytical instruments to perform routine adjustments and preventive maintenance. Such duties as module replacements, replumbing and simple servicing should be considered as the normal responsibility of the chemist. The more complex electronic servicing is generally the function of the electronics specialist.

D. SUMMATION:

The type of program discussed above requires an expenditure in man hours and/or money. Productive work output is somewhat reduced. The question should rightfully be asked "Is it worth the effort?" This may be answered in terms of the type of pesticide laboratory involved. In a laboratory primarily concerned with law enforcement, the analytical chemist may be called at any time as an expert witness to defend in court the accuracy and precision of his work on a given sample. Revelation of the lack of an active program of analytical quality assurance provides the opposition with valuable ammunition for discrediting the laboratory's case.

Pesticide laboratories concerned with the development of analytical data of a survey nature have a pressing responsibility to insure quality analytical performance. Generally, such laboratories are part of a network feeding data to a central point for processing. Erroneous data from one or more of the component laboratories of the network can lead to false conclusions concerning the pesticide profile of the sample material in the areas assigned to those errant laboratories. For example, let us assume that a laboratory assigned to the analysis of general population blood in a given area is consistently, but erroneously, finding higher pesticide levels than is being reported by laboratories in other areas. Plotted on a national scale, it would then appear that the people of this area contain higher levels of pesticides than the rest of the national population.

We think it appropriate to reiterate here the importance of periodic checking of pesticide profiles in substrates by confirmatory techniques. The reporting of pesticides not actually present is just as misleading as failure to identify pesticides which are present. By way of review, the following quote is taken from a memorandum issued from Perrine in September 1968, and entitled "CHANGES IN ANALYTICAL METHODOLOGY":

> "The identification of chlorinated insecticides and their metabolites will be confirmed in every 5th sample of adipose tissue analyzed in the respective laboratories. This will be accomplished primarily through the application of TLC and, where instruments are available, by microcoulometry. In order to enhance the sensitivity of the TLC procedure, we recommend using a combination of chromogenic agent and electron capture gas chromatography as outlined in Appendix A.
>
> In the Community Studies Laboratories where tissue samples are received in sets from the same individual, the confirmatory tests performed on the adipose tissue extract will stand as indirect evidence for the presence of these insecticides in the other tissues from that individual. The Micro-Mills procedure will continue to be used to survey the insecticide levels in tissues such as: gonad, liver, brain, etc.
>
> In order to obtain some indirect confirmation of the presence of chlorinated insecticides in blood, the following procedure will be used in the

National Monitoring and Community Studies Laboratories. Serum remaining after the regular Dale-Cueto analysis will be saved and pooled until 50 ml is accumulated. The Macro-Mills procedure will then be used to clean up an extract of this pooled serum sample which will then be analyzed by TLC and, where available, microcoulometry. The extraction method for the 50 ml serum sample is outlined in Appendix B. Analysis by TLC will be carried out as described for adipose tissue in Appendix A. The actual number of pooled samples to be analyzed will depend on the workload in the individual labs and should be worked out with the contract officer."

A properly functioning intralaboratory quality control program greatly reduced the possibility of any laboratory straying into a pattern of continuing error since the periodic recovery checks serve to flash a warning. The lack of such a program inspires little confidence in the routine data from any laboratory. When the analytical work program of a laboratory is planned, definite consideration must be given to the allowance of sufficient time to conduct a quality assurance program. A low total output of reliable analytical data is at least useful. An impressively high volume of uncontrolled data, however, is worse than none at all because of the distorted and misleading profile that could result.

Figure 1 PERIODIC CHECK LIST FOR GAS CHROMATOGRAPH (E.C. DETECTOR)

DAILY	WEEKLY	MONTHLY
1. Check response with standard mixture and relate to previous day.	1. Change glass wool plug at column inlet.	1. Clean recorder slide wire with Freon MS-180.
2. Change glass insert sleeve in injection port (end of day).	2. Change septums. (3)	2. Change pyrometer batteries and clean battery contacts with Freon MS-180
3. Check recorder electrometer zero and noise level at operating attenuation.	3. Run background current profile and polarizing voltage response curve.(4)	3. Check recorder speed at settings in normal use.
4. Check carrier gas flow rate through each column with bubble meter (early morning and afternoon).	4. If endrin is a compound of interest chromatograph pure standard at a concentration and attenuation that will produce a peak of 50 to 60% f.s.d.(5)	4. Check gas flow system for leaks using "SNOOP".(6)
5. Check temp. of detector, inlet, transfer and column oven.(1)	5. Check for any shifting of column packing resulting in forward movement beyond the bottom of column exit nut and/or settling in excess of 1/2" from glass wool inlet plug.	5. Evaluate performance of each column with special standard mixture (Fig. 3).
6. Chromatograph standard p,p'-DDT on each working column used at a concentration and attenuation that will produce a peak of 50 to 60% f.s.d.(2)		6. Check entire instrument for loose connections and frayed wire insulations.
		7. Check all rotameters and flow controllers for proper float action by the prescribed method.

---

(1) Oven temp. should be monitored by an outboard thermometer.

(2) The formation of p,p'-DDD and/or p,p'-DDE indicated on-columb breakdown.

(3) This frequency assumes use of improved silicone rubber. Old type requires more frequent changing.

(4) Daily check may be indicated if injecting large numbers of sample extracts.

(5) The formation of one or two additional peaks indicates on-column breakdown.

(6) Checks should be made whenever new detector or new tank of gas is installed, or whenever erratic baselines are observed.

PESTICIDES IN AIR

Anne R. Yobs, M.D.

There has been worldwide concern about pollution of the atmosphere with certain radioactive materials for more than 25 years. More recently localized concern has developed over pollution of the cities' air with carbon monoxide, certain hydrocarbons, sulfur compounds, smoke, dust, and many other malodorous and poisonous byproducts of combustion, although their presence in air is by no means limited to modern times. Problems pertaining to the pollution of the atmosphere have been intensively studied and technical as well as economically feasible remedial or control action has been proposed and actually undertaken for many of those pollutants the presence or effects of which are readily demonstrated. These materials become atmospheric pollutants incidental to or as waste products of combustion and other processes, usually from readily identifiable and rather localized sources.

Pesticide chemicals, on the other hand, are intentionally introduced into a broad segment of the environment for the sole purpose of controlling various pests. There is increasing evidence that pesticide pollution is now worldwide and its significance to the environment, while receiving widespread consideration, is not yet fully understood. Furthermore, the contribution that airborne pesticides make to the total environmental picture awaits definition as does their importance to man's health and well-being.

Pesticides may enter the air in several ways. These are drift from application procedures, volatilization from treated soil and plants or contaminated water, wind erosion of soil, domestic use of aerosols and thermal vapors, and incidental to industrial and disposal processes.

The problem of drift has been recognized for at least 25 years and probably even longer. The very first use of agricultural chemicals for pest control probably resulted in undesirable - and unrecognized - residues on adjacent crops, nearby households, persons or animals, and wildlife areas. The extent of the early drift problems was proportionate to the limited use and the methods of application of these chemicals. Obviously, a man carrying a sack of Paris green dust which he shook over each plant would not cause drift problems as extensive as those created by a powered ground duster or spray plane discharging 300-500 pounds dust per minute - a crop cover rate 1,000 times the hand operation. As early as 1927, California enacted regulations on chemical residues, including those which may result from drift. During the 1945-46 season, large amounts of calcium arsenate were used on tomatoes and the drift of this chemical caused the death of several dairy animals fed with hay from an adjacent alfalfa field.

The number of chemical formulations remained small for some years, but with the discovery of the hormone herbicides (2, 4-D and similar formulations) and their resulting widespread use, the drift problem became more acute and a number of crop dusting cases even reached appellate court during 1952-53, suggesting that numerous cases must have been filed in lower courts.

Three factors affecting each pesticide application are important in the physics of drift. These are (1) distribution equipment and method of use, (2) the physical form and formulation of the chemical applied, and (3) the microclimatology controlling dispersion of the material after discharge from the applicator and before it reaches the intended target.

Drift control work has placed emphasis on the aircraft applicator rather than the ground rig because major drift problems are more frequently associated with large scale operations requiring aircraft application. It is quite likely that large ground sprayers, especially those using air carrier means, may cause drift hazard commensurate with that from aircraft; however, there is greater control over a ground rig and the lower discharge rate has less drift potential.

Aircraft may be used to apply agricultural chemicals in various physical forms. Released material enters the air wake created by the wing in flight. This wake pattern carries the material outward toward the wing tips, then drops it in a swath which is about wing span width. Two distinct vortices develop at each wing tip and there is a distinct central propeller wash which skews the wake to one side of the aircraft's centerline. The pattern is similar but less sharply defined with helicopters. Above 15-20 m.p.h. helicopters do not develop any greater downwash than does the fixed wing aircraft. The vortex pattern is characteristic of both.

The particle size range for all physical forms (dusts, granules or sprays) depends on the initial screening during manufacture; this is especially true with dry materials. Dusts, for example, are screened to a range of 1-25μ with a stated average of 80-90% of the formulation under 25μ.

Large particles or droplets will travel through the air at fairly high speed and either deposit on the target or fall to the ground. In finer mist sprays with particle diameters of 20-50 microns, droplets will remain airborne for a longer period. Under some conditions the liquid carrier may evaporate, at least in part, resulting in even smaller particles of pesticides that may remain airborne still longer. Dusts and aerosols may contain still smaller particles, the latter as small as 2 microns diameter. Moreover some pesticides are applied as true vapor (particularly in fumigation processes) and thus remain airborne indefinitely or until they either decompose or are absorbed on some other material.

While many factors influence the movement of pesticides discharged from an aircraft, some idea of the drift pattern of various particle sizes can be obtained from Table I.

Table I[1]

Drop diameter microns	Particle type	Distance particle would be carried by a 3 m.p.h. wind, while falling 10 feet
400	Coarse aircraft spray	8.5 feet
150	Medium aircraft spray	22.0 feet
100	Fine aircraft spray	48.0 feet
50	Air carrier sprayers	178.0 feet
20	Fine spray and dusts	0.21 mile
10	Usual dusts and aerosols	0.84 mile
2	Aerosols	21.0 miles

Dusting has greater drift hazard and results in deposit of less active chemical than with other physical forms. Dusts are generally more expensive, both in initial cost and application cost on the basis of pounds of active material per acre. However, the formulation is fixed with no mixing required at the site of application and the total pounds applied per acre is usually less with dusts than with sprays.

Granular materials appear to offer the lowest drift hazard of any formulation; however, the usual size range (30-60 mesh or 600-200μ) does not adhere to plant surfaces, nor does the number of particles per pound of material provide sufficient coverage or spreading on the ground to insure contact with most insect species.

Spray applications offer a wide range of chemical formulation. Atomization or droplet size can be controlled by using various nozzle types, altering operating pressures and the discharge angle in relation to the plane's stream. Other important factors are such physical properties of the spray formulation as viscosity, density and surface tension.

After the material leaves the applicator device, local weather forces become important in the eventual deposit or drift loss of the chemical. These local factors include wind velocity and direction and turbulent mixing. The relative humidity of the surrounding air and its interrelation with evapotranspiration on the crop may also have significant influence on deposit behavior.

Volatilization of pesticides from treated soils and plants and contaminated water is dependent on complex interrelationships involving properties of the chemical, properties of the soil and the climate. Properties of the chemical which are important include aqueous solubility, vapor pressure, intrinsic stability of the compound. The absolute vapor pressures of the organochlorine insecticides are very low (Table II), yet volatilization is one of the most important causes of loss from the soil. This is enhanced in the presence of free water at the soil surface.

Table II[2]
Vapor Pressures of Organochlorine Insecticides

Insecticide	Vapor pressure at 20 C	Relative volatility
	mm Hg	
p,p'-DDT	1.0 X 10-7	Low
Dieldrin	1.0 X 10-7	Low
Aldrin	6.0 X 10-6	Medium
Lindane	9.4 X 10-6	Medium
Chlordane	1.0 X 10-5	Medium
Heptachlor	3.0 X 10-4	High

As the organic matter content of soil increases, vaporization decreases because of strong adsorption to the organic materials. Rates of vaporization are highest immediately following application before the pesticide has become completely adsorbed. Changes in the soil moisture level also affect volatilization through the mechanism of displacement of the chemical from the soil particle by water, which makes the chemical more susceptible to vaporization. While ambient conditions such as high temperature and high soil moisture could enhance volatilization, direct distillation of the pesticide onto the leaf may occur when leaf temperatures fall below those of the soil, as in radiation cooling at night, in the same way that dew is formed. Any procedure which increases the exchange of air, such as disking and harrowing treated soils, increases the rate of pesticide loss from the soil; conversely, pesticide loss is reduced where a cover crop provides shade or reduces air flow over the soil.

Vaporization of pesticides is not restricted to one season of the year but is a continuous process in areas that do not experience long periods of freezing weather or snow accumulation. The maximum rate of release undoubtedly is at the time of application of the pesticide or shortly thereafter. For pesticides in soils, however, the rate of release may rise again after the crop is harvested when a greater exchange of air is possible.

Pesticides are present in most major river systems of the U. S. and in nearly all major water bodies on the planet. The chlorinated hydrocarbons do not dissolve easily in water and they have a tendency to adsorb to any available surface and so cling to soil particles, to be removed by sedimentation. However, pesticides may also vaporize as a result of their tendency to accumulate at the surface of the water where they are carried off into the atmosphere as the water evaporates.

In 1966, Cohen and Pinkerton reported the transport of pesticide-laden dust through the atmosphere. This dust originated in a mammoth dust storm over the Southern High Plains west of Lubbock, Texas and was subsequently deposited by rainfall many hundreds of miles away 24 hours later. Results of analysis are given in Table III.

Table III[3]
Pesticide Content of Dust

Pesticide	Concentration, p.p.m.[a]
DDT (tech.)	0.6
Chlordan (tech.)	0.5
DDE	0.2
Ronnel	0.2
Heptachlor epoxide	0.04
2,4,5-T	0.04
Dieldrin	0.003
Total organic chlorine	1.34
Total organic sulfur	0.5

[a] Based on air-dried weight of dust.

Pesticides or related products may be discharged directly into the air through smokes and other clouds incidental to manufacturing or processing or in burning of "empty" containers, or even in the case of fires in warehouses and such situations. Wolfe et al. have reported finding as much as 7.9 mg./m^3 of parathion in such smoke.

The distribution and dispersion of airborne pesticides will depend on particle size and meteorological conditions as well as distance above ground at which they become airborne. Information on the dispersal and distribution of pesticides in the vapor phase or in the particle range below 5 microns is almost completely lacking.

Pollutants travel with the wind. Hourly wind observations at the ground level are available at many places. Unfortunately such weather stations are normally several hundred kilometers apart and good wind data in between is lacking. Further, wind information above 10 meters height is even less plentiful and pollutants travel with winds at higher levels. Wind patterns on a smaller scale can be quite complex and may be strongly influenced by surface characteristics, time of day, and associated temperature fluctuations, i.e., hills, mountains, lakes, large rivers and cities may cause characteristic vertical and horizontal patterns.[4]

Dispersion of a contaminant in the atmosphere essentially depends on two factors: mean wind speed, which reduces concentration with increased speed, and atmospheric turbulence, which through mixing of clean and contaminated air decreases contaminant concentration. Turbulence is formed by two mechanisms: heating from below and wind shear. Heating produces convection which occurs whenever temperature decreases rapidly. Mechanical turbulence just above the ground is common because there is no wind at ground level and there is usually some wind just above ground.

Within the past two years, two papers have been published which describe the first direct evidence that pesticides are part of the general atmospheric circulation and are being carried in the air thousands of miles in significant quantities. The first (Risebrough, 1968) dealt with the analysis of dust collected on glycerin-coated nylon screens erected on Barbados.[5] This island lies at the southeastern fringe of the West Indies and is exposed to the northeasterly trade winds blowing across the Atlantic from Africa and Europe. Indications were found that mineral and biological material in the dust had originated in Africa or Europe and traveled 3,000 miles or more across the open Atlantic. The dust contained dieldrin, DDT, DDE, and DDD. DDT was present in every sample throughout the yearlong study. Dieldrin was present in every season but not every sample.

The second paper reported the results of monitoring British rainwater for pesticides between August 1966 and July 1967.[6] Once again there are clear indications that pesticides were being transported across thousands of miles of ocean water - this time by westerlies from North America. The residues included BHC, dieldrin, DDT, DDD and occasional traces of heptachlor epoxide. There were seven sampling stations, ranging from Lerwick on the Shetland Islands more than 100 miles from the northern tip of Scotland and 200 miles west of Bergen, Norway, to Camborne at the southeast tip of England, a distance of 700 miles. Lerwick is more removed from any agricultural activity than any of the other stations but samples collected there showed comparable levels of dieldrin and the DDT group and the highest concentrations of BHC of any of the seven stations. Also, the total concentration of all pesticides was the highest recorded at any of the stations. These residues could hardly have had local origins. Residues of the BHC and DDT group were found during the entire year, dieldrin from August 1966 through January 1967. The highest concentrations occurred during the November-January quarter and included the highest quarterly concentrations of BHC and dieldrin reported at any of the seven stations.

Other studies have been interpreted by many as indirect evidence of the presence of airborne pesticides on a worldwide scale. These include the discovery of measurable levels of DDT in certain wildlife native to the Arctic and Antarctic.[7,8]

Although most research on pesticides air pollution has been directed toward the more obvious problems of agricultural drift and occupational exposure, there have been some studies to determine the pesticide burden of ambient air. It is difficult, however, to compare results from one study to another because of differences in sampling location, substrate sampled (air, dust fall or rainwater), sampling method and interval, and analytical procedure. An accurate determination of pesticide concentrations in air has been complicated by the difficulty of collecting residues which exist in both particulate and vapor phase. Many methods used have been adaptations of methods originally used in sampling air for other pollutants.

Tabor used a high volume sampler equipped with a glass fiber filter to sample particulate pesticides in 1963 and 1964.[9] This system functioned at a flow rate of 73,000 cubic feet per day, and levels of pesticides were found to run as high as 8,000 nanograms/m^3 during fogging operations. This system included no provision for trapping vapors nor for measuring the loss due to volitization of trapped particulate pesticides.

Abbott et al. measured the levels of organochlorine pesticide residues in rainwater collected at monthly intervals on roofs of two buildings approximately 1.45 km. apart in central London.[10] These materials were thought to be present as a result of atmospheric scrubbing by the rain.

Cohen and Pinkerton, cited earlier, examined samples of dust deposited in Cincinnati, Ohio on January 26, 1965.[3]

Bamesberger and Adams collected 24-hour air samples of air impinged on air imfaction discs rotating through a N-decave collecting fluid to retain droplets of impacted aerosols. The gaseous fraction was collected in a modified midget impinger containing a two-phase N-decave and 3 percent aqueous sodium bicarbonate solution.[11] These were examined for 2,4-D and 2,4,5-T).

Detectable levels of particulate DDT were observed by Autommaria et al. in the air in Pittsburgh using a sampling procedure which divided the dust particulates into two size categories, respirable and nonrespirable.[12]

An extensive program of monitoring of ambient air for concentrations of pesticides was performed in 1967-68 by the Midwest Research Institute for the Pesticides Program of the U. S. Public Health Service.[13] Air monitoring stations were set up at 9 localities in various parts of the country and air was sampled for one week during a baseline period and for 2 of every 4 weeks during the estimated usage period for the area, to a total of 6 months sampling. A sampling series consisting of coarse fiberglass filtercloth, Smith Greenburg impinger with solvent and alumina adsorbent was used. Results are summarized in Table IV.

A similar but more extensive program of regular air sampling is now being performed by the Division of Pesticide Community Studies.[14] The same sampling equipment is being used with only the fiberglass cloth prefilter and a solvent. The solvent being used now is ethylene glycol. Samples were collected at 15 different urban and rural locations in 1970. Measurable amounts of these pesticides were detected in one or more samples:

the DDT group, including op' and pp'DDT, pp'DDE and/or pp'DDD
Dieldrin
Endrin
Aldrin
Heptachlor
alpha BHC
gamma BHC
Thiodan
Diazinon
Methyl Parathion
Ethyl Parathion
Malathion
Ronnel
2,4-D Butoxy ethyl ester

Temporal and geographic variation in qualitative and quantitative aspects of airborne pesticides have been noted. Levels of some materials have been unexpectedly high.

TABLE IV

MAXIMUM PESTICIDE LEVELS FOUND IN AIR SAMPLES

(Levels in ng/cu m.)

Pesticides	Baltimore (123 Samples)	Buffalo (57 Samples)	Dothan (90 Samples)	Fresno (120 Samples)	Iowa City (94 Samples)	Orlando (99 Samples)	Riverside (94 Samples)	Salt Lake City (100 Samples)	Stoneville (98 Samples)
p,p'-DDT	19.5 (89)*	11.0 (40)	177.0 (88)	11.2 (62)	2.7 (56)	1560 (99)	24.4 (85)	8.6 (62)	950 (98)
o,p'-DDT	3.0 (59)	2.9 (24)	88.0 (72)	5.5 (28)	2.1 (21)	500 (95)	6.2 (44)	1.4 (29)	250 (98)
p,p'-DDE	2.4 (4)		13.2 (32)	6.4 (3)	3.7 (10)	131 (29)	11.3 (6)		47 (76)
o,p'-DDE			3.9 (13)			9.6 (7)			1.9 (25)
α-BHC	4.5 (27)			4.5 (4)	4.4 (9)			9.9 (30)	
Lindane	2.6 (4)				0.1 (1)			7.0 (24)	
β-BHC	2.2 (4)							1.8 (3)	
δ-BHC								9.9 (5)	
Heptachlor					19.2 (37)	2.3 (7)			
Aldrin					8.0 (1)				
Toxaphene			68.0 (11)			2520 (9)			1340 (55)
2,4-D								4.0 (1)	
Dieldrin						29.7 (50)			
Endrin									58.5 (25)
Parathion						465 (37)			
Methyl parathion			29.6 (9)			5.4 (3)			129 (40)
Malathion						2.0 (4)			
DEF									16 (12)

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* Number of samples containing detectable amounts of the pesticide.

Problem oriented air sampling, especially that directed to determination of levels to which workers are exposed presents a different type problem which is both simpler and more complicated. Sampling devices which have been used by various authors include midget impingers, impactor-scrubbers and various pads or patches attached to the worker's clothing or placed in his respirator. One difficult problem is the extrapolation of these values to a reflection of total exposure. Chemical analysis is somewhat easier since levels are higher than those usually encountered in ambient air samples and interest is generally limited to one or a few compounds which are known to be present.

While it is important that the atmosphere is a reservoir of pesticide residues which is undergoing constant modification and which regularly returns pesticides to the earth's surface on land and water, it should be remembered that mammals are exposed to these airborne materials through respiration, ingestion, and skin contact. Respiratory and dermal exposure are extremely important routes of absorption for many pesticide chemicals. The effect of airborne pesticides on man's health and on the total environment warrants further investigation.

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Pesticides and Carcinogenesis

Richard R. Bates

In a consideration of the carcinogenicity of pesticides, we are primarily interested in whether or not commercially used pesticides are carcinogenic for man. At this point, it should be stated that there is no good evidence that pesticides have induced cancer in man. However, it is not adequate to stop at this point. The absence of firm, positive evidence does not necessarily mean that there is strong negative evidence. In evaluating the potential risk of cancer to humans exposed to pesticides, it is useful to ask several questions. Are there any studies in humans relating pesticide exposure to cancer? What is the experimental evidence for carcinogenicity or lack of carcinogenicity of pesticides? On the basis of the latent period for the development of tumors from humans exposed to known carcinogens, when would we expect to find an increased incidence of cancer in humans exposed to carcinogenic pesticides?

Most of the better sources of information on the latent period for chemical carcinogenesis in man come from occupational exposures to carcinogens. The first report of occupational carcinogenesis was the result of astute clinical observations by an English surgeon, Percivall Pott (1). In 1775, he reported that there was a high incidence of cancer of the scrotum in chimney sweeps. These individuals entered the trade as young boys. Pott reported that he had never seen a case before puberty, but he did not indicate the age at which most cases occurred. Thus, it seems that the minimum latent period for the development of cancer of the scrotum in chimney sweeps was several years. More precise information on latent period is shown in Figure I giving data from Hueper and Conway (2). Before 1900, chimney sweeps in England still began their employment as children. The peak incidence for scrotal cancer was 35 years or more after the beginning of exposure, though a few cases developed within 15 or 20 years. Following 1900, the minimum age of employment was raised to 18 years and consequently the age at which most cancers developed was somewhat later.

Another industry associated with a high incidence of scrotal cancer was the cotton industry. During the second half of the nineteenth century and the early part of the twentieth century, cotton was spun on a machine which was lubricated with mineral oil. While tending these machines, workmen were continually sprayed with the mineral oil in the inguinal region. Figure II shows the time after beginning of employment at which these workmen developed cancer of the scrotum (3). The first few cases had a latent period of 15 to 20 years but the maximum incidence was not reached until approximately 50 years. In looking at these figures today it seems inexcusable that an occupational hazard of this type should have been allowed to continue for such a long time. However, if a similar situation should arise today, how long would it take us to recognize that there was a problem and to identify the carcinogen involved? The answer to this depends on the circumstances. It is easiest to identify the problem if several cases of a rare type of cancer develop in a population served by the same physician or same medical group. It is more difficult if the carcinogen increases the incidence of a common type of cancer which would be expected to occur several times in the population under observation of the physician or if the population exposed to the carcinogen has such varied sources of medical care that no one physician is apt to see more than a single case of cancer induced by the carcinogen. In the case of cancer of the scrotum shown here, an industry physician seeing two cases should be alerted to the possibility that the workmen are exposed to a chemical carcinogen since cancer of the scrotum is rare in the general population. However, if the carcinogen were to induce a more common type of cancer such as lung cancer, it would probably take many more cases to arouse the suspicion of the industry physician. The problem of workmen exposed to pesticides in the manufacturing process is similar to the problem shown here. The chance of identifying a carcinogenic hazard to agricultural workers is reduced because of the scarcity of large, stable groups having unified medical care. Thus, even if uncommon types of cancer are induced by a chemical carcinogen, it will take a long time to suspect a hazard if the size of the population at risk which is seen by any single physician is so small that he is not apt to see more than one case every few years.

One of the most potent human carcinogens to have been described is 2-Naphthylamine. This was used in the dyestuff industry. Among the workmen exposed to this compound, the incidence of bladder tumors rose to as high as 40%. Figure III shows the time required from the beginning of exposure to the development of tumors (4). Substantial numbers of cases arose between 5 and 10 years while the mean period was 17.8 years.

Workmen at nickel refineries have been observed to have a high incidence of cancer of the lung and of the nose (5). Figure IV shows the latent period for the induction of these types of cancer in workmen employed at a refinery in Wales. As in the other cases that we have seen, the latent period is a matter of years with the peak incidence between 20 and 25 years for cancer of the nose and between 25 and 30 years for lung cancer.

Finally, let us look at the latent period for carcinoma of the lung and bronchus, a disease which in most cases has cigarette smoking as an etiologic agent. Figure V shows that the maximum mortality rate from cancer of the lung and bronchus occurs at age 70 while the first noticeable rise in the curve is at age 40 (6). Since most cigarette smokers begin the habit at least by their early twenties, few cases develop with less than 20 years exposure.

Thus, these examples show that a noticeable rise in human cancer would take several years after the onset of exposure in the case of the most potent human carcinogens, while with many other, less potent carcinogens it might require several decades of observation in order to detect carcinogenicity.

These considerations lead to the question, "Have humans been exposed to individual pesticides for a sufficient length of time that we can consider the absence of epidemiologic data on carcinogenicity to indicate that these pesticides are in fact not carcinogenic for man at the levels of human exposure?" A major change in pesticide usage began in 1945. Before this time pesticides consisted largely of inorganic compounds and of natural products. Arsenicals played a large role. There is some clinical and epidemiologic evidence suggesting the induction of cancer of the skin by arsenic (7), though arsenic containing compounds have not been shown to be carcinogenic for experimental animals. DDT became available commercially in 1945 and this began the era of widespread use of synthetic, organic pesticides. Figure VI shows the United States production of synthetic, organic pesticides, growth regulators, and other similar agricultural products from 1945 to 1968. The figures from 1950 through 1968 come from the U. S. Tariff Commission (8) while that from 1945 is from a publication of the U. S. Department of Commerce (9). The figures in these two sources may not be strictly comparable. Nevertheless, it is apparent that the production of synthetic, organic pesticides has risen very dramatically from 1945 to the present time. This, of course, is a composite of the production of many individual chemicals. DDT was produced for military use for several years before 1945. Its production rose to a maximum of 188 million pounds in 1963 and has fallen off somewhat since then (10). Many other pesticides have come on the market in more recent years. Thus, with synthetic, organic pesticides, the time since the beginning of human exposure is less than 30 years for DDT and a considerably shorter period for many other pesticides. When we compare this time period with the latent periods for cancer development after exposure to known human carcinogens, we can conclude that if DDT were as potent a human carcinogen as 2-Napthylamine, it should be possible to detect this by now among the workmen involved in the manufacture of this insecticide since the early years of its manufacture if this is a stable population of workers with good medical observation. If DDT is a weak human carcinogen, it might not be possible to detect this carcinogenicity by the present time even in a stable industrial population. Other, more recently developed pesticides may not have had time to induce a detectable increase of tumors in man even if they are fairly strong carcinogens.

If we now turn to the question of the carcinogenicity of pesticides for man or for experimental animals, the most striking thing is the absence of good data in the literature. This subject was reviewed by the Advisory Panel on Carcinogenicity of Pesticides of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health (11). In the report of that commission, it is estimated that there are now on the order of 900 pesticidal chemicals. The Panel on Carcinogenicity found published reports on the chronic toxicity of only about 90 pesticides. It went on to indicate the likelihood that a substantial number of the remaining pesticides had undergone some such studies but that these are in the files of industry and of the Food and Drug Administration and are not readily available to the general scientific public. Of the reports which were evaluated, the Panel had this to say, "The quality of evidence in some of the reports was another source of difficulty. Many of the reports, published and unpublished, failed to provide enough data to permit judgments as to the safety of some pesticides. Details of the experiments (numbers of animals, description of controls, duration of the experiments) were sometimes missing." Thus, even among the published experiments, there was often insufficient data for the reader to draw his own conclusions about the carcinogenicity or lack of carcinogenicity of the chemicals tested. When the available literature was examined, the Panel found only three pesticides which had adequately been tested in a second species. Thirteen pesticides were concluded to be positive for tumor induction while twenty-eight gave some indication that they might increase the incidence of tumors in the experimental animals but the data was not sufficiently strong for the Panel to reach the conclusion that they were definitely carcinogenic. This leaves 800 or more pesticides with no adequate published experiments which could be used to evaluate whether or not they are carcinogenic. Many of these 800 probably consist of pesticides having very little use and thus of potential hazard to only a very small proportion of the population. However, many pesticides in wide usage are also among those having no adequate published experiments. Among these are malathion, parathion, trifluralin, toxaphene, pichloram, paraquat, and quite a few others.

If the literature on animal experiments for carcinogenicity is depressingly inadequate, the data in man is no better. On this subject, the Panel on Carcinogenicity had this to say, "The relationship between pesticides and chronic disease, including cancer, has not been adequately studied in man. A review of available literature, including a Medlars search, reveals that most studies to date were done on small sample sizes, for short periods of time, and without adequate follow-up." I shall not discuss this literature in any detail but simply refer you to Chapter 4 on the effects of pesticides on man and Chapter 5 on carcinogenicity of pesticides of the Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health. The best studies available on man are with DDT, aldrin, and dieldrin. All three of these pesticides have been found to be tumorigenic in mice when fed for long periods of time at high dose levels. The currently available studies on man with these three pesticides are essentially negative (11) except for one autopsy study indicating a higher concentration of DDT in the fat of patients dying with some kinds of cancer than in accidental death (12). The interpretation of this observation is complicated by the fact that DDT concentrations in the fat of an individual losing weight increase. On the basis of the information now available, it seems likely that these three pesticides are not as great a hazard to man as 2-napthylamine, but the data are not sufficient to rule out the possibility that they are weak carcinogens affecting a relatively small proportion of the exposed population after a long latent period.

Now let us take a look at the experimental data on the carcinogenicity of pesticides. The evidence for the carcinogenicity of all thirteen pesticides which were considered positive by the Panel on Carcinogenesis was based on experiments in mice. One pesticide, aramite, was also carcinogenic in the dog. Although in some cases there was suggestive evidence in the rat, none of this was conclusive. In most cases, the tumors were found after a long latent period of about 1½ years (13). Thus, exposure was for a major portion of the lifespan of the animal before tumors developed. This is in contrast to many of the potent chemical carcinogens used in laboratory experiments on chemical carcinogenesis which in some cases induced tumors within a few months or less (2, 7). Thus, the suggestion from the mouse data is that those pesticides which have been found to be carcinogenic are weakly carcinogenic. However, there are complicating factors which make this interpretation appear to be somewhat superficial. For example, although aramite required a major portion of the lifespan of the mouse to induce hepatomas in a relatively small proportion of the animals, a large proportion of dogs fed aramite developed cancer of the gall bladder and bile ducts beginning less than 2½ years after the beginning of feeding of this pesticide (14). This is similar to the situation with 2-napthylamine, our example of a potent human occupational carcinogen. Tumors were induced in dogs after a latent period corresponding to a short proportion of the lifespan whereas this carcinogen has induced tumors in rodents after a latent period corresponding to a much larger portion of the lifespan (15, 16). These two examples, aramite and 2-napthylamine, should not be taken as an indication that the dog tends to be susceptible to carcinogenesis and rodents resistant. Other chemicals could be chosen to demonstrate a reverse relationship. However, they do demonstrate the problem in attempting to draw a conclusion as to the relative carcinogenicity of chemicals from experiments done in one species.

The problem of species differences is always a problem in toxicology when animal experiments are used as an indication of relative safety or hazard of chemicals for man. Sometimes it is possible to detect species differences in the metabolism of a particular chemical and to correlate these differences with differences in toxicity. If this can be done, it is then possible to determine the human metabolism of the chemical and thus to determine the likelihood that it is toxic for man. A good example of this is the carcinogen 2-acetylaminofluorene. This chemical was originally developed as a pesticide but fortunately its potent carcinogenicity was discovered during early toxicity tests so that it was never marketed. 2-acetylaminofluorene is carcinogenic for the rat but not for the guinea pig. Studies on its metabolism revealed that the nitrogen atom is hydroxylated in the rat but not in the guinea pig. It was then observed that N-hydroxyacetylaminofluorene is carcinogenic for both the rat and the guinea pig (17). Thus, it appears that N-hydroxylation is an essential step in the activation of 2-acetylaminofluorene to make it carcinogenic. Studies in humans have revealed that man can hydroxylate 2-acetylaminofluorene (18). Thus, it is very likely that this chemical is a human carcinogen.

There are many other examples which illustrate the principle that the apparent potency of a chemical carcinogen depends upon the experimental circumstances under which it is tested. I shall select a few examples of these complicating factors from the literature on skin carcinogenesis since this is the field in which most of my own work has been done. However, it would be equally possible to find comparable examples of effects on tumor development in other organs.

Tannenbaum showed that restricting the caloric intake of mice reduced the yield of skin tumors induced by benzo(a)pyrene (19). Dietary levels of specific nutrients can also affect the incidence of tumors induced by chemical carcinogens (7).

Many experiments have shown that hormone levels affect the tumor yield (7). In my own laboratory we found that male mice were much more susceptible to the induction of skin tumors by 7,12-dimethylbenz(a)anthracene than female mice. The susceptibility of the females could be increased by removing their ovaries. It was also found that the susceptibility of the females fluctuated during the estrous cycle. They were more susceptible when the carcinogen was applied during diestrous than during other times in the cycle (20).

In the usual form of toxicity experiments, the animals are treated with one chemical while efforts are made to prevent cross-contamination and exposure of the animals to other chemicals. This contrasts with the human situation in which there is simultaneous and sequential exposure to many different chemicals. That this constitutes a major problem in interpretation of dose response relationships is shown by two types of experiments. The first of these is known as the two-stage system of skin carcinogenesis. Berenblum and Shubik (21,22) treated mice with a single dose of a polycyclic hydrocarbon carcinogen at a level which was too low to induce tumors. However, if these animals were then given multiple weekly applications of croton oil, a noncarcinogenic but irritating plant extract, a high yield of tumors developed. Thus, a dose of the chemical carcinogen which by itself was noncarcinogenic resulted in a high yield of tumors if the animals were subsequently exposed to another chemical. Another example of this type is shown in Fig. VII. Bingham and Falk found that when a .02% solution of benzo(a)pyrene dissolved in decalin was applied to the skin three times per week half the animals developed skin tumors. When the concentration of the carcinogen was reduced by a factor of 10, no tumors developed. In contrast, when the benzo(a)pyrene was dissolved in equal amounts of N-dodecane and decalin, 93% of the mice developed tumors from treatment with a 0.02% concentration of the carcinogen and a 1000 fold dilution of the carcinogen still induced tumors in 21% of the mice treated. It was only when a 10,000 fold dilution of the carcinogen was made that no tumors developed.

Thus, carcinogenicity experiments in animals are useful to indicate which chemicals have the proper molecular configuration to make them carcinogenic. Both qualitative and quantitative differences in metabolism among different species make it likely that some chemicals found to be carcinogenic in experimental animals will be noncarcinogenic for man and conversely that some human carcinogens may be noncarcinogenic for any particular species selected for testing. The many types of interactions which affect the quantitative results of a carcinogenesis experiment make it impossible to estimate a "threshold level", and even relatively crude estimates of comparative potency of chemical carcinogens can only be made after multiple experiments under varied conditions in several species of animals.

I am afraid I have not been able to give many definitive answers to the many questions involving the carcinogenicity of pesticides, but such is the state of our knowledge today. In concluding, I can do no better than to quote from the chapter on the Effects of Pesticides on Man in the Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health. "To sum up, the field of pesticide toxicology exemplifies the absurdity of a situation in which 200,000,000 Americans are undergoing life-long exposure, yet our knowledge of what is happening to them is at best fragmentary and for the most part indirect and inferential. While there is little ground for forebodings of disaster, there is even less for complacency (11)".

Figure 1

AGE DISTRIBUTION OF SCROTAL CANCER IN CHIMNEY SWEEPS*

Years	1892 (Cases)	1935 (Cases)
25-35	4	1
36-45	7	6
46-55	14	18
56-65	4	33
66-75	--	28
76-85	--	17
Average Age	45-50	61.9

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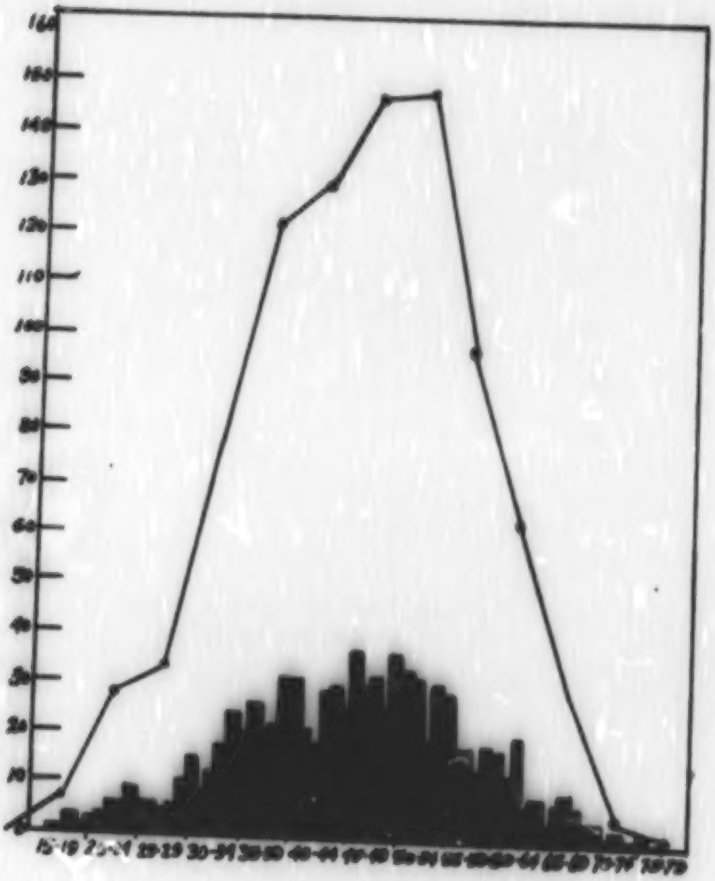
* Hueper, W.C., Conway, W.D., Chemical Carcinogenesis and Cancers Charles C. Thomas, Springfield, Illinois, 1964, Page 86

Fig. II - Time from beginning of exposure to mineral oil until development of scrotal cancer among mule spinners *



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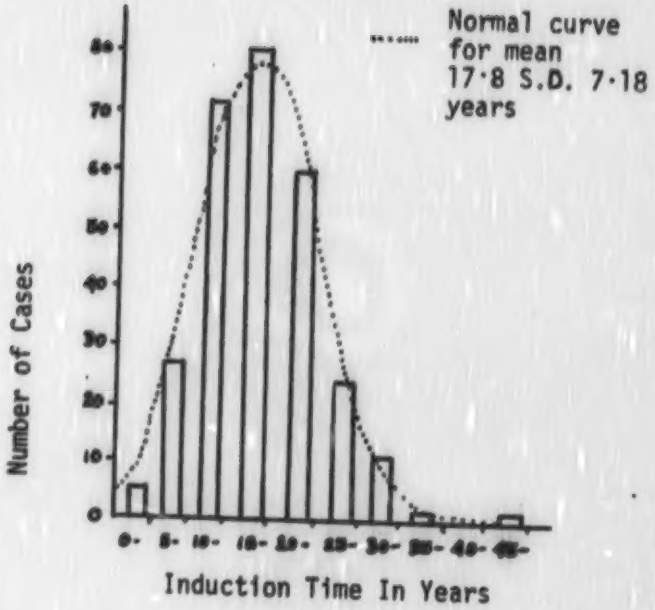
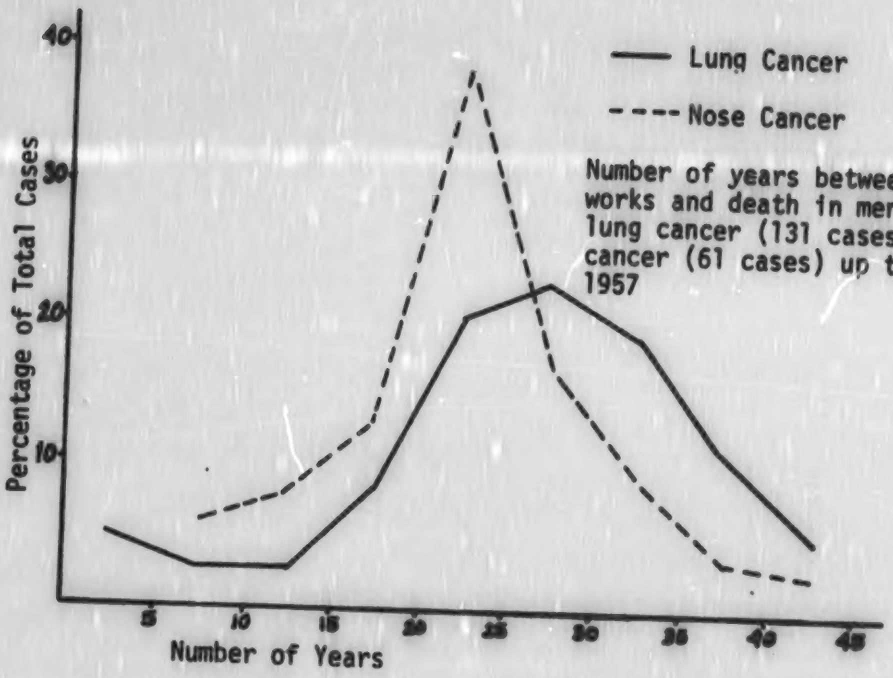
* Henry, S.A., Cancer of the Scrotum in Relation to Occupation, Oxford University Press, New York, 1946, Page 83

Fig. III - Incidence of Bladder Tumour in the Dyestuffs Industry *



* Case, R.A.M., Hosker, M.E., McDonald, D.B.,
Tumours of the Urinary Bladder in Workmen Engaged in the Manufacture and Use of Certain Dyestuff Intermediates in the British Chemical Industry
British Journal of Industrial Medicine
1954, Volume 11, Page 75

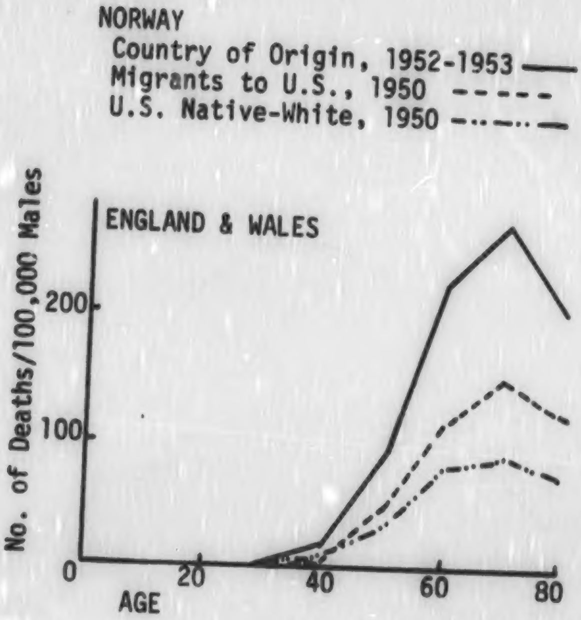
Fig. IV Nickel Workers*



Number of years between entry to works and death in men dying of lung cancer (131 cases) and nose cancer (61 cases) up to December 31, 1957

* Morgan, J.G., Some Observations on the Incidence of Respiratory Cancer in Nickel Workers , British Journal of Industrial Medicine, 1958, Volume 15, Page 224

Fig. V Lung and Bronchus, Males *



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* Haenszel, W., "Quantitative Evaluation of the Etiologic Factors in Lung Cancer", from Tobacco and Health by James, G. and Rosenthal, T.(ed.) Charles C. Thomas, Springfield, Illinois, 1962, Page 267

Fig. VI Synthetic Organic Pesticides
U.S. Production

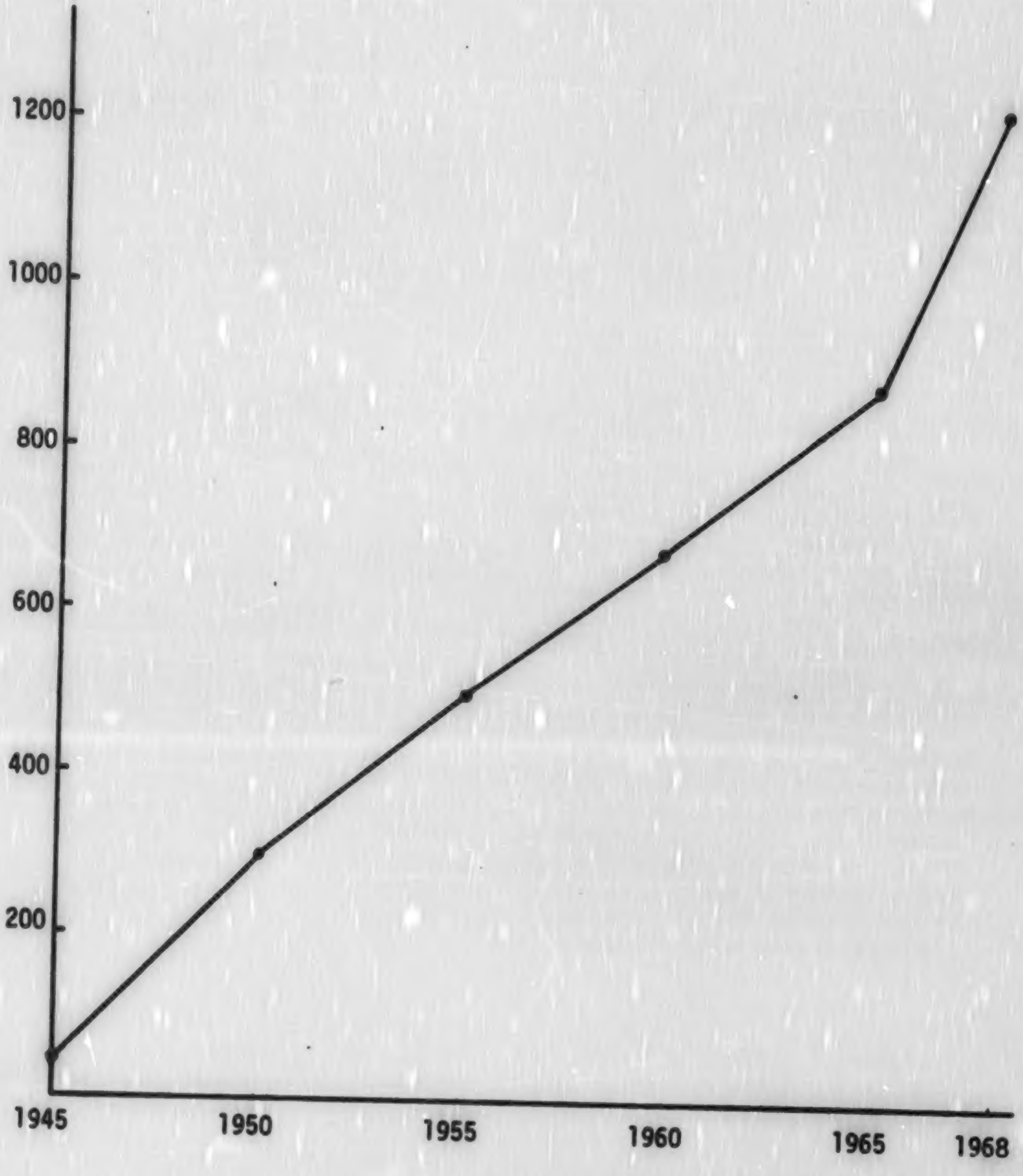

Fig. VII - The Results of Repeated Cutaneous Applications of Low Concentrations of Benzo[a]pyrene in Decaline or n-Dodecane and Decalin ***

Solution*	Original No. of Mice	No. Alive at 50 wks	Av Latent Period (wks)	No. of Mice Developing Tumors		Incidence of Tumors (%)
				Malignant	Benign	
0.02% benzo[a]pyrene in decalin	20	12	58	5	1	50
0.02% benzo[a]pyrene in n-dodecane & decalin+	20	16:	25	10	5	93
0.002% benzo[a]pyrene in decalin	30	20	...	0	0	0
0.002% benzo[a]pyrene in n-dodecane & decalin	30	26:	48	7	2	35
0.0002% benzo[a]pyrene in decalin	30	21	...	0	0	0
0.0002% benzo[a]pyrene in n-dodecane & decalin	30	23	64	3	3	26
0.00002% benzo[a]pyrene in decalin	30	18	...	0	0	0
0.00002% benzo[a]pyrene in n-dodecane & decalin	30	24	80	5	0	21
0.000002% benzo[a]pyrene in n-dodecane & decalin	30	24	...	0	0	0
n-dodecane & decalin	40	30	...	0	0	0

* Dosage, 50 mg three times per week.

+ n-dodecane and decalin, 50:50 by weight.

: Number alive after 50 weeks is given for those groups not developing tumors prior to 1 year of treatment. Final effective number (FEN) given for the two groups that developed a substantial number of tumors before 1 year. The FEN is the number of mice alove at the median time of the occurrence of tumors plus any of those that had died previously with a tumor.

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HEAVY METALS

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Basically, the heavy metals in food chemicals and foods are defined as metallic impurities colored by the sulfide ion. They are normally quantified by a parallel comparison with a standard lead solution, and expressed in terms of lead, ppm of the test substance. Elements included in this group are Pb, Hg, Cu, Cd, As, Sb, and Sn. However, in recent years, because of the Japanese poisoning episodes involving fish contaminated with mercury and rice with cadmium, and the experimental work of Schroeder and others on abnormal trace metals, e.g., Pb, As, Cd, Te, it is recognized that detailed information is needed about the levels of each heavy or non-essential metal in foodstuffs. Basically, the hazard of heavy metals intake is related to the fact they may accumulate in tissues and cause biochemical abnormalities leading to chronic disorders. Although foods are the major source of man's intake of heavy metals, other sources of exposure--air and water--may also be important. Further, the presence of heavy metal residues in foodstuffs is essentially part of a much greater problem, involving the cycling of heavy metals in nature. This in many ways resembles the problems associated with persistent pesticides. However, whereas the organic pesticides present in the biosphere result entirely from man's activities, man's contribution of heavy metals to the biosphere may be small compared to the amount derived from the lithosphere and hydrosphere. At present very little is known about global cycles involving heavy metals. For total environmental cycles, information is needed on the geology and wearing of rocks, global chemical contamination of air, water and soil from human activities, accumulation and metabolism by plants and animals, and finally the effects of excesses and deficiencies on health and disease of man and animals.

Although it is likely that only in extreme cases (such as methyl mercury poisoning in the Minamata episode) that the morbidity of heavy metals diffused through the community will reach levels corresponding to serious effects, it is possible that a level of poisoning may occur which at present cannot be recognized, since these effects ressemble many other clinical or subclinical situations.

Consequently, there is a great need for research in the quantitative and retrospective estimation of exposure to heavy metals in amounts below the level to produce marked clinical symptoms. Applications of epidemiological studies to communities with concomitant studies of levels of heavy metals in tissues are required.

Mercury, lead and cadmium will be used as examples to examine some of these problems.

MERCURY

Mercury is usually discharged into the environment in one of the following forms: (a) as metallic mercury, (b) the inorganic divalent ion (e.g., mercuric chloride), (c) aryl mercury (e.g., phenylmercuric acetate), (d) alkyl mercury (e.g., methyl mercury dicyandiamide), and (e) alkoxyalkylmercury (e.g., methoxyethyl mercury acetate).

Symptoms and signs of poisoning with short chain alkyl mercury salts and mercury vapors differ from those of other mercury compounds. They are characterized by effects on the central nervous system, and correspondingly high levels of mercury compared to other mercurials are found in the central nervous system. In the case of aryl mercury compounds and alkoxymercury compounds, symptoms are similar to those described for inorganic mercury, and are characterized by salivation, stomatitis and erethism with much less evidence of motor or sensory nerve affection. Usually in cases of chronic exposure to these compounds, death occurs from kidney damage before brain levels are high enough.

Although acute mercury poisoning is rare and chronic intoxication affecting the nervous system is rarely seen, concern for the extremely hazardous nature of mercury residues in foodstuff has been emphasized by the Minamata Bay and Niigata mercury poisoning episodes, and more recently by the extent of mercury in the Scandinavian, Baltic and United States aquatic environment. Essentially, the problem is related primarily to the fact that all forms of mercury entering the aquatic environment may be converted to methyl mercury, which is more toxic chronically than other forms of mercury, and can be concentrated by fish and other aquatic species. In addition there is the possibility of the direct introduction of alkyl mercurials into the food chain through the misuse of mercury-treated seeds. Air and water are not significant sources of mercury for non-industrially exposed persons.

Entry of Mercury Into the Biosphere:

The entry of mercury into the aquatic environment may be through man-made contamination resulting from its use in mercury-cell-type chlor-alkali plants or slimicidal discharges from pulp manufacturing plants, mercury-type pesticides, or other miscellaneous sources including refuse from hospitals, laboratories, dental clinics, discarded electrical appliances, fungi-resistant paints. The burning of fossil fuels has also been implicated in the general problem of mercury contamination. The presence of mercury in isolated bodies of water may be due to geological formations which release mercury through the process of leaching or volatilization. The natural methylation of mercury occurs in sediments in river and lake bottoms. The process can result in the formation of monomethyl or dimethyl mercury. The conversion is thought to occur through the action of methanogenic bacteria. High concentrations of mercury and acid pH appear to favor the formation of monomethyl mercury, whereas alkaline conditions favor the formation of dimethyl mercury. Since the latter is more volatile than the monomethyl form, and may not be accumulated by fish, its production may favor the release of mercury into the atmosphere. Microbial systems also degrade organic mercury to elemental mercury. However, its role in nature is not known. At present the significance of these various factors in the movement of mercury in the biosphere is not known. It seems likely that the vaporized dimethyl mercury and elemental mercury play an important role in the cycling of mercury among the air, soil and water components of the environment.

As regards the direct introduction of alkyl mercurials into other foodstuffs, this problem is directly related to the misuse of mercury-treated seed for animal feed and the ingestion of such seed by game birds. The ability of mammalian species to convert mercury compounds to alkyl mercurials has not been established. However, it is possible that hens may be able to convert mercury compounds to alkyl mercurials. Although foliar treatment of plants, e.g., rice, with mercurial compounds leads to high concentration of mercury in plant tissues, the chemical form of the mercury has not been established. Translocation of mercury from treated seed does not produce significant contamination of the harvested grain.

Toxic Effects of Mercury:

Any evaluation of the potential hazard of mercury residues in foods should distinguish between alkyl, aryl and inorganic mercury. Although organic mercurials are acutely less toxic than inorganic mercurials, chronically the organic mercurials, particularly the alkyl mercurials, are more toxic. Several factors may contribute to this effect: (a) relative amounts of mercury absorbed, and (b) major differences in metabolism. Less than 2% of a dose of inorganic mercury may be absorbed, whereas methyl mercury is completely absorbed. Both alkyl and aryl mercurials are absorbed unchanged. Animal studies have provided valuable information on the differences in metabolism between alkyl and aryl mercury salts, equilibrium states, and critical concentrations of methyl mercury required to produce neurological effects. Following administration of inorganic mercury, accumulation occurs mainly in the kidney and liver with lesser amounts in other tissues. Accumulation in brain is extremely slow. Phenyl mercuric acetate causes a more pronounced accumulation of mercury in the liver and intestines, with lesser amounts in the renal cortex. With methyl mercury the distribution of mercury in the tissues is more uniform. Further, there is a slow but pronounced accumulation of mercury in the brain. A unique property of methyl mercury is its ability to cross the placental barrier. Distribution of blood mercury between the erythrocytes and plasma is also dependent on the type of mercury administered, e.g., following administration of inorganic mercury, only 25% of the mercury is bound to the erythrocyte, whereas, for methyl mercury, approximately 90% (depending on species) is bound. At present the significance of these binding mechanisms on subsequent metabolism and distribution of mercury is not known.

Metabolic studies in animals with organic mercurials show that phenyl mercuric acetate is rapidly metabolized in the liver and kidneys. Following a single dose, unchanged phenylmercury can be detected only for 96 hours. In contrast in a similar study with ethylmercury, unchanged ethylmercury was detectable in liver and kidneys for 21 days. Further, the fecal excretion of mercury over a 7-day period following administration of ethylmercury was only one-twentieth of that observed in the phenylmercury study. The stability of alkyl mercurials and the slow rate of excretion has been further demonstrated in equilibrium studies. Repeated subcutaneous injection of rats with phenylmercuric acetate results in a steady state in about 2 weeks. With methylmercury equilibrium is not reached after 6 weeks. However, in the case of continuous feeding studies at dietary dose levels of 0.2 to 5 ppm, equilibrium was reached at all dose levels in about 6 months, corresponding to a daily excretion of 2% of the body burden. The concentration of mercury in the brain also reaches equilibrium with respect to the general body burden of mercury. Studies with mice have shown that a critical concentration of mercury in brain is required to produce effects. Concentrations of mercury more than 30 μg/g tissue was associated with death following neurological symptoms, whereas survival with neurological symptoms was possible with 20 μg/g tissue. Eight μg mercury/g brain tissue is considered a 'no effect' level. The information derived from equilibrium rates between body burden and rates of excretion and blood and brain levels of mercury in animals and man have been used as a basis for determining acceptable levels of methyl mercury in the diet.

Another serious aspect of methyl mercury residues in foods is the ability of this compound to cross the plancental barrier. The placental transfer of methyl mercury has been clearly demonstrated using autoradiographic techniques. In addition, congenital cerebellar atrophy has been produced in the offsprings of pregnant animals treated with methyl mercury.

The mutagenic properties of mercury compounds have been demonstrated in Drosophila and Allium roots, but not in experimental animals.

The available information on the effect of mercurials in man has been mainly derived from industrial exposure and accidental poisoning and more recently from the poisoning due to mercury in fish in Minamata Bay (1953-1960) and Niigata, Japan (1964). In addition, a great deal of work has been done in Scandinavia, relating methyl mercury intake in man to observable blood levels. A study with human volunteers, receiving a single dose of mercury-203 labelled methyl mercury, showed that for man, the half-life of methyl mercury is 70 days. About 10% of the radioactivity was located in the head region. Excretion, which was mainly in the feces, was about 1% per day. No cases of poisoning due to ingestion of fish have been reported in Scandinavia or the United States.

The levels of mercury in fish in Minamata Bay at the time of the poisoning episode was estimated to be 10 to 20 ppm. Fish consumption in this area is very high, with an estimated average daily intake of 200 g. In the United States the estimated average daily intake of fish is 14 g. Blood mercury levels of intoxicated persons in the Japanese episodes were as high as 1300 ppb (whole blood). The lowest blood mercury level at which intoxication occurred was 200 ppb (whole blood). However, this value may be low, because there is no definite information on the time between measurement of blood level and exposure to methyl mercury. Average blood mercury values for Swedish individuals consuming fish once a week were approximately 5.5 ppb. Studies in 20 individuals in the Lake St. Clair (Michigan) area, eating fish from twice weekly to twice monthly, indicate blood mercury levels of 7 ppb to 51.5 ppb with an average value of 17.8 ppb. Some Scandinavian individuals consuming high levels of contaminated fish have blood levels exceeding 200 ppb but have not exhibited any toxic manifestations. There appears to be a direct relationship between blood levels of mercury and intake of fish containing methyl mercury residues. It is estimated that an intake of 0.3 mg methyl mercury/day produces a total blood level of 200 ppb.

In addition to blood levels, hair levels of mercury may be a useful indicator of human exposure. The values reported for mercury hair levels in intoxicated cases in Japan was higher than 500 ppm. The mercury hair level for an average fish eater (Swedish and Canadian) is approximately 8 ppm. In individuals at equilibrium there is a direct relationship between the mercury level in blood and hair.

At present there are no good biochemical parameters for predicting preclinical effects. Whole blood levels and hair levels of mercury are the best available indicators of exposure to methyl mercury. The Food and Drug Administration guideline level of 0.5 ppm Hg in the raw edible portion of fish and shellfish provides a sound basis to protect consumers against high mercury levels arising from environmental contamination.

LEAD

Entry in the Biosphere:

Lead is one of the more common elements occurring in the earth's crust. In addition to contamination of the environment by the leaching of geological formations, information published in the Mineral Handbook of 1966 indicated that man's activity in the United States alone added approximately 700,000 tons of lead to the environment in that year. The contribution of lead from tetraethyl lead to the environment was estimated to be 185,250 tons. This would be exhausted into the atmosphere to be either inhaled directly or deposited in vegetation, soil and water. The available information indicates that contamination of soils and vegetation from air pollution is directly related to traffic volume and distance from the highway. Further, since the ratio of lead in vegetation to that in soils is much higher where the source of lead is from automobile exhaust rather than from geologic sources, plants may absorb lead directly from the atmosphere. Only a minor part of the lead released from tetraethyl lead settles and accumulates in the vicinity of the roads. Lead found in the surface waters of oceans and other remote areas can be attributed to gasoline.

However, the increased contamination of the environment does not appear to have caused a marked increase in dietary lead during the past 20 to 30 years. Measurements of levels of lead in milk, which reflect an integrated exposure of the cow to lead, may be considered as useful indicators of lead levels in the environment. These levels have shown only a very slight increase during the past 20 to 30 years. Water pollution may result in accumulation of lead in fish. However, the concentration factor for lead may be low compared with that of other heavy metals, e.g., 35 for ocean fish, 15 for fresh water fish and 1050 for clams.

At present there is little information about any natural mechanisms that could be involved in the cycling of lead in the environment. Although volatile organic lead compounds are readily synthesized, there is no indication that these are formed in nature. In fact there is little information on the chemical nature of lead in living organisms and foodstuffs.

Toxicity of Lead:

The potential hazards from the consequences of exposure of the general population to lead has been of concern for some time. Although the available information indicates that the man's intake of lead is mainly derived from food (approximately 0.3 mg/day), other sources include water (up to 0.02 mg/day) and air (approximately 0.04 mg/day, based on values for New York City air, 2 $\mu g/m^3$ and breathing at a rate of 20 m^3/day). However, the amount of ingested lead absorbed is small, approximately 7%. There is still considerable controversy as to the contribution of inhaled lead to the total body burden of lead. Inhaled lead may be readily absorbed (up to 40%) and this may contribute to amounts equal to that absorbed from the diet. Although the chemical nature of lead in food has not been established, the metabolic pattern resembles that of inorganic lead salts. Most of the lead in the atmosphere is in the form of elemental lead, with only a small amount present as unchanged tetraethyl lead. In contrast to inorganic lead, tetraethyl lead is primarily neurotoxic and does not cause anemia. The available data indicate that the amount of tetraethyl lead present in the atmosphere is toxicologically insignificant and does not contribute to the body burden of lead.

There is still uncertainty as to the possible effects on human health of the present normal exposure to lead. The acute and chronic effects of lead toxicity in adults and children have been characterized and duplicated in experimental animals. However, the mild symptoms of lead poisoning are difficult to recognize; 80 µg lead/100 ml blood has previously been accepted as a level below which clinical poisoning does not occur. However, lower levels may have been suggested, particularly for children, where the upper safe level may be 50 to 60 µg lead/100 ml blood. Problems relating to the evaluation of the safety of the present dietary intake of lead are concerned with the total amount of the lead that may be accumulated in the body, and also the criteria used to determine an effect level. An effect level may be either a clinical or biochemical change in human subjects. For example, measurements of the most sensitive biochemical parameter of exposure to lead, namely, erythrocyte δ-aminoleuvulinic acid dehydrase, indicate that in Finland inhibition of this enzyme occurs under normal urban conditions. However, although the significance of this change is not known, it demonstrates that even the comparatively low exposure to lead prevailing today may interfere with metabolism.

CADMIUM

Entry Into the Biosphere:

Metal mining and smelting operations are a major source of cadmium pollution. However, these effects may be localized in specific areas where the levels of metals, presumably in the form of dust settling on vegetation, may reach near toxic levels for grazing animals. Ground water in mining areas may also be contaminated. Other sources of cadmium in the atmosphere include manufacturing processes involving cadmium and the use of cadmium pigments. Measurements of cadmium in dustfall indicate that 1-2 grams of cadmium is deposited per acre each year. The role of air pollution as a direct contributor to the body burden does not appear to be of any significance. However, its role in increasing the amount of cadmium available for uptake by plants and its contribution to water supplies and subsequent entry into the food chain are not known.

In addition to the uptake of cadmium by plants from natural geologic sources, it has been suggested that the use of super-phosphates, which have relatively high cadmium concentration, may contribute to cadmium levels in plant products. However, there is no definite indication that this occurs.

Cadmium in the aquatic environment is known to be accumulated by shellfish.

Toxicology:

The detailed studies of Schroeder and others have shown that cadmium excess can produce hypertensive disease in animals, and that same problem may apply to humans. In man, one of the most typical findings in chronic cadmium poisoning is the excretion of specific proteins of low molecular weight in the range of 2×10^4 to 3×10^6. The proteinuria is largely due to irreversible damage of the kidney tubules. Recently, a chronic form of cadmium poisoning, 'Ouchi-Ouchi,' has been described in Japan. This was caused by eating contaminated foods and beverages. The normal daily intake of cadmium in the diet is 200 - 400 μg/day. In the case of the Japanese poisoning episode, analyses of rice and soya beans grown in the area showed that the rice had cadmium levels of 0.44 - 3.36 ppm, and soya beans, 1 ppm. The total cadmium intake from a diet containing 400 g rice and 100 g soya beans range from 240 - 1440 μg/day. Only small amounts of ingested cadmium are absorbed, and less than 1 or 2% accumulates in the body, mainly in the soft tissues.

At present the only form of cadmium in foodstuffs (plant and animal tissues) is unknown except for the Cd-Zn protein, metallothionen, found in the kidney. The bioavailability of the forms of cadmium in foodstuffs has yet to be established.

FDA PROGRAMMES RELATED TO THE PROBLEM OF METAL CONTAMINATION OF FOODS

Programmes directly related to heavy metals in fish and other food products include:

1) Mercury and other heavy metals in fish.
2) Mercury in other foods.
3) Mercury-treated seeds.
4) Arsenic, mercury, and cadmium in the total diet.
5) Metals in shellfish.
6) Lead in pottery.

A programme for metals in fish is currently under development, which would involve surveying fish from various waters for 12 metals (lead, arsenic, cadmium, selenium, chromium, cobalt, nickel, zinc, antimony, copper, tin and manganese). In order to determine if other foods contribute significant amounts of mercury to the diet, ten selected commodities are being studied:

(1) Flour (wheat), (2) non-fat dry milk, (3) sugar, (4) potatoes, (5) raw ground beef, (6) chicken breasts, (7) shrimp, (8) beef liver, (9) shell eggs and (10) fluid whole milk. In addition, Food and Drug Administration is continuing the study of certain metals (As, Cd, and Hg) in foods on a total diet study. These studies are concerned with the normal dietary intake of residues and take into account geographical and seasonal aspects.

Toxicological studies are underway to assess the various aspects of alkyl mercury poisoning in prenatal, neonatal, and postnatal beagle dogs and miniature swine, and prenatal rats and hamsters.

In addition, there is a continuing programme on the toxicological aspects of cadmium. Investigations are underway on the effect of nutrients in either increasing or decreasing the adverse effects of cadmium.

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